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=> e andersen peter/au

E1	6	ANDERSEN PERNILLE/AU
E2	1	ANDERSEN PETE/AU
E3	329 -->	ANDERSEN PETER/AU
E4	4	ANDERSEN PETER A/AU
E5	1	ANDERSEN PETER ANDREAS/AU
E6	5	ANDERSEN PETER B/AU
E7	59	ANDERSEN PETER C/AU
E8	1	ANDERSEN PETER CHRISTIAN/AU
E9	3	ANDERSEN PETER CRAIG/AU
E10	62	ANDERSEN PETER E/AU
E11	1	ANDERSEN PETER ESKIL/AU
E12	1	ANDERSEN PETER ESKILD/AU

=> s e3-e12 and tuberculosis

L1 236 ("ANDERSEN PETER"/AU OR "ANDERSEN PETER A"/AU OR "ANDERSEN PETER ANDREAS"/AU OR "ANDERSEN PETER B"/AU OR "ANDERSEN PETER C"/AU OR "ANDERSEN PETER CHRISTIAN"/AU OR "ANDERSEN PETER CRAIG"/AU OR "ANDERSEN PETER E"/AU OR "ANDERSEN PETER ESKIL"/AU OR "ANDERSEN PETER ESKILD"/AU) AND TUBERCULOSIS

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 124 DUP REM L1 (112 DUPLICATES REMOVED)

=> s l2 and (rd1?

UNMATCHED LEFT PARENTHESIS 'AND (RD1?'

The number of right parentheses in a query must be equal to the number of left parentheses.

=> s l2 and (rd1?)

L3 14 L2 AND (RD1?)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 14 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 AN 2004:345624 BIOSIS  
 DN PREV200400347773  
 TI Reactivation of **tuberculosis** during immunosuppressive treatment  
 in a patient with a positive QuantiFERON(R)-**RD1** Test.  
 AU Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase Bengaard;  
 Lundgren, Bettina; Nielsen, Lars N.; Lillebaek, Troels; Soerensen, Inge  
 J.; **Andersen, Peter**; Weldingh, Karin  
 CS Hvidovre HospDept Infect Dis, Univ Copenhagen, Kettegards Alle 30,  
 DK-2650, Hvidovre, Denmark  
 pravn@dadlnet.dk  
 SO Scandinavian Journal of Infectious Diseases, (July 2004) Vol. 36, No. 6-7,  
 pp. 499-501, 497. print.  
 CODEN: SJIDB7. ISSN: 0036-5548.  
 DT Article  
 LA English  
 ED Entered STN: 18 Aug 2004  
 Last Updated on STN: 18 Aug 2004  
 AB A patient with polymyositis developed **tuberculosis** during  
 immunosuppressive treatment. Tuberculin Skin Test and chest X-ray failed  
 to demonstrate latent **tuberculosis**, whereas a blood sample that  
 was tested with a modified QuantiFERON(R)-TB-assay, using the recombinant  
 ESAT-6 and CFP-10, was positive indicating that this patient was latently  
 infected before immunosuppressive therapy. This case indicates the risk  
 of progressing from latent to active **tuberculosis** given that the  
 subject is **RD1** responsive, and we believe that preventive  
 anti-tuberculous treatment could have prevented this case of  
**tuberculosis**. We suggest that **RD1** based tests are  
 evaluated further in immunocompromised patients.  
 TI Reactivation of **tuberculosis** during immunosuppressive treatment  
 in a patient with a positive QuantiFERON(R)-**RD1** Test.  
 AU . . Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase  
 Bengaard; Lundgren, Bettina; Nielsen, Lars N.; Lillebaek, Troels;  
 Soerensen, Inge J.; **Andersen, Peter**; Weldingh, Karin  
 AB A patient with polymyositis developed **tuberculosis** during  
 immunosuppressive treatment. Tuberculin Skin Test and chest X-ray failed  
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 latently infected before immunosuppressive therapy. This case indicates  
 the risk of progressing from latent to active **tuberculosis** given  
 that the subject is **RD1** responsive, and we believe that  
 preventive anti-tuberculous treatment could have prevented this case of  
**tuberculosis**. We suggest that **RD1** based tests are  
 evaluated further in immunocompromised patients.  
 IT . . . and Homeostasis); Infection; Methods and Techniques  
 IT Parts, Structures, & Systems of Organisms  
 blood: blood and lymphatics, analysis  
 IT Diseases  
**tuberculosis**: bacterial disease, diagnosis, etiology  
**Tuberculosis** (MeSH)  
 IT Methods & Equipment  
 QuantiFERON-**RD1** test: clinical techniques, diagnostic  
 techniques, laboratory techniques; immunosuppressive therapy: clinical  
 techniques, immunologic techniques, laboratory techniques, therapeutic  
 and prophylactic techniques; tuberculin. . .  
 ORGN . . . Mammals, Primates, Vertebrates  
 ORGN Classifier  
 Mycobacteriaceae 08881  
 Super Taxa  
 Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;  
 Bacteria; Microorganisms  
 Organism Name  
 Mycobacterium **tuberculosis** (species): pathogen  
 Taxa Notes  
 Bacteria, Eubacteria, Microorganisms

L3 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 AN 2004:76163 BIOSIS  
 DN PREV200400078267  
 TI Human T-cell responses to the **RD1**-encoded protein TB27.4  
 (Rv3878) from Mycobacterium **tuberculosis**.  
 AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei Meng;  
 Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; **Andersen,**  
**Peter**  
 CS Department of Infectious Disease Immunology, Statens Serum Institut,  
 Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
 eag@ssi.dk  
 SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.  
 CODEN: IMMUAM. ISSN: 0019-2805.  
 DT Article  
 LA English  
 ED Entered STN: 4 Feb 2004  
 Last Updated on STN: 4 Feb 2004  
 AB In recent years, there has been considerable focus on the discovery and  
 characterization of proteins derived from Mycobacterium  
**tuberculosis** leading to the identification of a number of  
 candidate antigens for use in vaccine development or for diagnostic  
 purposes. Previous experiments have demonstrated an important  
 immunological role for proteins encoded by the **RD1** region, which  
 is absent from all strains of bacillus Calmette-Guerin (BCG) but present  
 in the genomes of virulent *M. bovis* and *M. tuberculosis*.  
 Herein, we have studied human T-cell responses to the antigen encoded by  
 the putative open reading frame (rv3878) of the **RD1** region.  
 Immunoblot analysis revealed that rv3878 was expressed and the native  
 protein was designated TB27.4. Immunological evaluations demonstrate that  
 TB27.4 elicits a prominent immune response in human **tuberculosis**  
 patients with a dominant region in the C-terminal part of the molecule.  
 In contrast, very limited responses were seen in *M. bovis* BCG-vaccinated  
 donors. This study therefore emphasizes the diagnostic potential of  
 proteins encoded by the **RD1** region.  
 TI Human T-cell responses to the **RD1**-encoded protein TB27.4  
 (Rv3878) from Mycobacterium **tuberculosis**.  
 AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei Meng;  
 Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; **Andersen,**  
**Peter**  
 AB In recent years, there has been considerable focus on the discovery and  
 characterization of proteins derived from Mycobacterium  
**tuberculosis** leading to the identification of a number of  
 candidate antigens for use in vaccine development or for diagnostic  
 purposes. Previous experiments have demonstrated an important  
 immunological role for proteins encoded by the **RD1** region, which  
 is absent from all strains of bacillus Calmette-Guerin (BCG) but present  
 in the genomes of virulent *M. bovis* and *M. tuberculosis*.  
 Herein, we have studied human T-cell responses to the antigen encoded by  
 the putative open reading frame (rv3878) of the **RD1** region.  
 Immunoblot analysis revealed that rv3878 was expressed and the native  
 protein was designated TB27.4. Immunological evaluations demonstrate that  
 TB27.4 elicits a prominent immune response in human **tuberculosis**  
 patients with a dominant region in the C-terminal part of the molecule.  
 In contrast, very limited responses were seen in *M. bovis* BCG-vaccinated  
 donors. This study therefore emphasizes the diagnostic potential of  
 proteins encoded by the **RD1** region.  
 IT  
 T-cell: blood and lymphatics, immune system  
 IT Diseases  
 Mycobacterium bovis infection: bacterial disease, infectious disease  
 Mycobacterium Infections (MeSH)  
 IT Diseases  
 Mycobacterium **tuberculosis** infection: bacterial disease,  
 infectious disease  
 Mycobacterium Infections (MeSH)  
 IT Chemicals & Biochemicals  
 BCG vaccine: immunologic-drug, immunostimulant-drug; TB27.4:

**RD1-encoded protein**

ORGN

ORGN Classifier

Mycobacteriaceae 08881

Super Taxa

Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;  
Bacteria; Microorganisms

Organism Name

Mycobacterium bovis (species): pathogen

Mycobacterium **tuberculosis** (species): pathogen

Taxa Notes

Bacteria, Eubacteria, Microorganisms

GEN Mycobacterium **tuberculosis** rv3878 gene (Mycobacteriaceae):  
expression

L3 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2004:33002 BIOSIS

DN PREV200400035432

TI PPE protein (Rv3873) from DNA segment **RD1** of Mycobacterium

**tuberculosis**: Strong recognition of both specific T-cell epitopes  
and epitopes conserved within the PPE family.

AU Okkels, Limei Meng [Reprint Author]; Brock, Inger; Follmann, Frank; Agger,  
Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik;  
Rosenkrands, Ida; **Andersen, Peter**

CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300, Copenhagen, Denmark  
lmo@ssi.dk

SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123.  
print.

ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 7 Jan 2004

Last Updated on STN: 7 Jan 2004

AB Proteins encoded by DNA segment **RD1** of Mycobacterium

**tuberculosis** have recently been demonstrated to play important  
roles in bacterial virulence, vaccine development, and diagnostic reagent  
design. Previously, we characterized two immunodominant T-cell antigens,  
the early secreted antigen target (ESAT-6), and the 10-kDa culture filtrate  
protein (CFP10), which are encoded by the *esx-lhp* operon in this region.  
In the present study we characterized a third putative open reading frame  
in this region, *rv3873*, which encodes a PPE protein. We found that the  
*rv3873* gene is expressed in *M. tuberculosis* H37Rv and that the  
native protein, Rv3873, is predominantly associated with the mycobacterial  
cell or wall. When tested as a His-tagged recombinant protein, Rv3873  
stimulated high levels of gamma interferon secretion in peripheral blood  
mononuclear cells isolated from **tuberculosis** (TB) patients, as  
well as from healthy tuberculin purified protein derivative-positive  
donors. In contrast to other **RD1**-encoded antigens, Rv3873 was  
also found to be recognized by a significant proportion of Mycobacterium  
bovis BCG-vaccinated donors. Epitope mapping performed with overlapping  
peptides revealed a broad pattern of T-cell recognition comprising both  
TB-specific epitopes and epitopes also recognized by BCG-vaccinated  
donors. The immunodominant epitope (residues 118 to 135) for both TB  
patients and BCG-vaccinated individuals was found to be highly conserved  
among a large number of PPE family members.

TI PPE protein (Rv3873) from DNA segment **RD1** of Mycobacterium

**tuberculosis**: Strong recognition of both specific T-cell epitopes  
and epitopes conserved within the PPE family.

AU . . . [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie;  
Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida;  
**Andersen, Peter**

AB Proteins encoded by DNA segment **RD1** of Mycobacterium

**tuberculosis** have recently been demonstrated to play important  
roles in bacterial virulence, vaccine development, and diagnostic reagent  
design. Previously, we characterized . . . frame in this region,  
*rv3873*, which encodes a PPE protein. We found that the *rv3873* gene is  
expressed in *M. tuberculosis* H37Rv and that the native protein,

Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other **RD1**-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of Mycobacterium bovis BCG-vaccinated donors. Epitope mapping performed.

IT . . . and Homeostasis)

IT Parts, Structures, & Systems of Organisms  
peripheral blood mononuclear cell: blood and lymphatics, immune system

IT Diseases  
**tuberculosis**: bacterial disease, infectious disease  
**Tuberculosis** (MeSH)

IT Chemicals & Biochemicals  
DNA segment **RD1**; PPE protein; T-cell antigens; T-cell epitopes; culture filtrate protein 10 [CFP10]; early secreted antigen target 6 [ESAT-6]; epitopes; esx-lhp operon; . . .

ORGN Classifier  
Mycobacteriaceae 08881  
Super Taxa  
Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms  
Organism Name  
Mycobacterium **tuberculosis** (species): strain-H37Rv  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

GEN Mycobacterium **tuberculosis** rv3873 gene (Mycobacteriaceae)

L3 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
AN 2000:282183 BIOSIS  
DN PREV200000282183  
TI Antigenic equivalence of human T-cell responses to Mycobacterium **tuberculosis**-specific **RD1**-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.

AU Arend, Sandra M. [Reprint author]; Geluk, Annemieke; van Meijgaarden, Krista E.; van Dissel, Jaap T.; Theisen, Michael; **Andersen, Peter**; Ottenhoff, Tom H. M.

CS Department of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden, Netherlands

SO Infection and Immunity, (June, 2000) Vol. 68, No. 6, pp. 3314-3321. print. CODEN: INFIBR. ISSN: 0019-9567.

DT Article  
LA English  
ED Entered STN: 6 Jul 2000  
Last Updated on STN: 7 Jan 2002

AB The early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of **tuberculosis**. Both antigens are encoded by **RD1**, a genomic region present in all strains of Mycobacterium **tuberculosis** and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 can be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of M. **tuberculosis**-specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost completely correlated ( $r = 0.96$ ,  $P < 0.0001$  for ESAT-6;  $r = 0.98$ ,  $P < 0.0001$  for CFP-10). More importantly, the same was found when gamma interferon production by peripheral blood mononuclear cells in response to these stimuli was analyzed ( $r = 0.89$ ,  $P < 0.0001$  for ESAT-6;  $r = 0.89$ ,  $P < 0.0001$  for CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with M. **tuberculosis**. The peptides in

DT Article  
 LA English  
 OS Genbank-AF004671  
 ED Entered STN: 3 Feb 1999  
 Last Updated on STN: 3 Feb 1999

AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by *Mycobacterium tuberculosis*. Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated *tuberculosis* vaccine strain *Mycobacterium bovis* BCG. The promoter region of *M. tuberculosis* esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the *M. tuberculosis* genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using *M. tuberculosis* RNA. The corresponding promoter signals were not recognized in *Mycobacterium smegmatis*, in which transcription of lhp/esat-6 is initiated at different locations. The *M. tuberculosis* lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in *M. tuberculosis* and that both code for small exported proteins.

TI A *Mycobacterium tuberculosis* operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10).

AU Berthet, Francois-Xavier [Reprint author]; Rasmussen, Peter Birk; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte

AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by *Mycobacterium tuberculosis*. Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated *tuberculosis* vaccine strain *Mycobacterium bovis* BCG. The promoter region of *M. tuberculosis* esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the *M. tuberculosis* genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using *M. tuberculosis* RNA. The corresponding promoter signals were not recognized in *Mycobacterium smegmatis*, in which transcription of lhp/esat-6 is initiated at different locations. The *M. tuberculosis* lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in *M. tuberculosis* and that both code for small exported proteins.

IT Major Concepts  
 Bacteriology; Infection; Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Diseases  
*tuberculosis*: bacterial disease  
 Tuberculosis (MeSH)

IT Chemicals & Biochemicals  
 early secreted antigenic target 6 kDa protein [ESAT-6]: T-cell protein antigen; CFP-10 protein: identification, low-molecular-mass culture filtrate protein; *Mycobacterium tuberculosis* esat-6 gene [early secreted antigenic target 6 kDa protein gene]: characterization, transcription, promoter region, operon, cloning; *Mycobacterium tuberculosis* lhp gene: identification, operon, transcription

ORGN  
 Mycobacteriaceae 08881  
 Super Taxa  
 Mycobacteria; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms  
 Organism Name  
*Mycobacterium bovis*: strain-BCG, vaccine strain  
*Mycobacterium smegmatis*  
*Mycobacterium tuberculosis*: pathogen  
 Taxa Notes

each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixtures of synthetic overlapping peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with *M. tuberculosis*, and peptides have the advantage of faster production at lower cost.

TI Antigenic equivalence of human T-cell responses to *Mycobacterium tuberculosis*-specific RD1-encoded protein antigens ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides.

AU Arend, Sandra M. [Reprint author]; Geluk, Annemieke; van Meijgaarden, Krista E.; van Dissel, Jaap T.; Theisen, Michael; **Andersen, Peter**; Ottenhoff, Tom H. M.

AB. . . early secreted antigenic target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising antigens for reliable immunodiagnosis of **tuberculosis**. Both antigens are encoded by RD1, a genomic region present in all strains of *Mycobacterium tuberculosis* and *M. bovis* but lacking in all *M. bovis* bacillus Calmette-Guerin vaccine strains. Production and purification of recombinant antigens are. . . be replaced with corresponding mixtures of overlapping peptides spanning the complete amino acid sequence of each antigen. Proliferation of *M. tuberculosis*-specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixtures were almost. . . CFP-10). Whole protein antigens and the peptide mixtures resulted in identical sensitivity and specificity for detection of infection with *M. tuberculosis*. The peptides in each mixture contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to. . . peptides have potency equivalent to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with *M. tuberculosis*, and peptides have the advantage of faster production at lower cost.

IT . . . System (Chemical Coordination and Homeostasis); Infection

IT Parts, Structures, & Systems of Organisms  
T-cell; peripheral blood mononuclear cell

IT Diseases  
**tuberculosis**

IT **Tuberculosis** (MeSH)

IT Chemicals & Biochemicals  
HLA-DR; culture filtrate protein-10; early secreted antigenic target 6-kDa

ORGN . . . Mammals, Primates, Vertebrates

ORGN Classifier

Mycobacteriaceae 08881

Super Taxa

Mycobacteria; Actinomycetes and Related Organisms; Eubacteria;  
Bacteria; Microorganisms

Organism Name

*Mycobacterium tuberculosis*

Taxa Notes

Bacteria, Eubacteria, Microorganisms

L3 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 1999:28278 BIOSIS

DN PREV199900028278

TI A *Mycobacterium tuberculosis* operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10).

AU Berthet, Francois-Xavier [Reprint author]; Rasmussen, Peter Birk; Rosenkrands, Ida; **Andersen, Peter**; Gicquel, Brigitte

CS Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724 Paris Cedex 15, France

SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203.  
print.

ISSN: 1350-0872.

## Bacteria, Eubacteria, Microorganisms

L3 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:490265 CAPLUS

DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN **Andersen, Peter**; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

PA Den.

SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY

PRAI DK 1997-376 A 19970402

US 1997-44624P P 19970418

DK 1997-1277 A 19971110

US 1998-70488P P 19980105

US 1998-50739 A2 19980330

DK 1998-1281 A 19981008

EP 1998-913536 A3 19980401

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN **Andersen, Peter**; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

ST sequence Mycobacterium culture filtrate antigen gene; *tuberculosis* vaccine diagnosis Mycobacterium culture filtrate antigen gene

IT 213992-10-0P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(*M. tuberculosis* culture filtrate antigen CFP29 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis)

IT 706035-97-4P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP30A N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-24-6P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP30B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-20-2P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP50 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-21-3P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP7B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-11-1P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP5A N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-89-4P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CFP5B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-13-3P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(M. **tuberculosis** culture filtrate antigen CWP32 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-88-3P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-23-6 706035-25-8 706035-27-0 706035-29-2 706035-31-6  
706035-33-8 706035-35-0 706035-37-2 706035-39-4 706035-41-8  
706035-43-0 706035-45-2 706035-47-4 706035-49-6 706035-51-0  
706035-53-2 706035-55-4 706035-57-6 706035-59-8 706035-61-2  
706035-63-4 706035-65-6 706035-67-8 706035-69-0 706035-71-4  
706035-73-6 706035-75-8 706035-77-0 706035-79-2 706035-81-6  
706035-83-8 706035-85-0

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-87-2

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-22-5 706035-24-7 706035-26-9 706035-28-1 706035-30-5  
706035-32-7 706035-34-9 706035-36-1 706035-38-3 706035-40-7  
706035-42-9 706035-44-1 706035-46-3 706035-48-5 706035-50-9  
706035-52-1 706035-54-3 706035-56-5 706035-58-7 706035-60-1  
706035-62-3 706035-64-5 706035-66-7 706035-68-9 706035-70-3  
706035-72-5 706035-74-7 706035-76-9 706035-78-1 706035-80-5  
706035-82-7 706035-84-9

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-86-1

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-03-5 706036-04-6 706036-05-7 706036-06-8 706036-07-9  
706036-08-0 706036-09-1 706036-10-4 706036-11-5 706036-12-6  
706036-13-7 706036-14-8 706036-15-9 706036-16-0 706036-17-1  
706036-18-2 706036-19-3 706036-20-6 706036-21-7 706036-22-8  
706036-23-9 706036-24-0 706036-25-1 706036-26-2 706036-27-3  
706036-28-4 706036-29-5 706036-30-8 706036-31-9 706036-32-0  
706036-33-1 706036-34-2 706036-35-3 706036-36-4 706036-37-5  
706036-38-6 706036-39-7 706036-40-0 706036-41-1 706036-42-2  
706036-43-3 706036-44-4 706036-45-5 706036-46-6 706036-47-7  
706036-48-8 706036-49-9 706036-50-2 706036-51-3 706036-52-4  
706036-53-5 706036-54-6 706036-55-7 706036-58-0 706036-59-1  
706036-60-4 706036-61-5 706036-62-6 706036-63-7 706036-64-8  
706036-65-9 706036-66-0 706036-67-1 706036-68-2 706036-69-3  
706036-70-6 706036-71-7 706036-72-8 706036-73-9 706036-74-0  
706036-75-1 706036-76-2 706036-77-3 706036-78-4 706036-79-5

RL: PRP (Properties)

(unclaimed nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-56-8 706036-57-9 706036-80-8 706036-81-9

RL: PRP (Properties)

(unclaimed protein sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as v

#### SYSTEM LIMITS

EXCEEDED

L3 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:60336 CAPLUS

DN 140:144681

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

IN **Andersen, Peter**; Rosenkrands, Ida; Stryhn, Anette

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006952	A2	20040122	WO 2003-DK477	20030708
	WO 2004006952	A3	20040318		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP	1523331	A2	20050420	EP 2003-763613	20030708
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US	2004057963	A1	20040325	US 2003-617038	20030711
PRAI	DK 2002-1098	A	20020713		
	US 2002-401725P	P	20020807		
	WO 2003-DK477	W	20030708		
AB	The present invention is based on a number of M. <b>tuberculosis</b> derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.				
TI	Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of <b>tuberculosis</b>				
IN	<b>Andersen, Peter</b> ; Rosenkrands, Ida; Stryhn, Anette				
AB	The present invention is based on a number of M. <b>tuberculosis</b> derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.				
ST	Mycobacterium <b>tuberculosis</b> low oxygen induced antigen gene vaccine diagnostic				
	; BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)				
	(γ; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of <b>tuberculosis</b> )				
IT	650674-04-7P	650674-05-8P	650674-06-9P	650674-07-0P	650674-08-1P
	650674-09-2P	650674-10-5P	650674-11-6P	650674-12-7P	650674-13-8P
	650674-14-9P	650674-15-0P	650674-16-1P	650674-17-2P	650674-18-3P
	650674-19-4P	650674-20-7P	650674-21-8P	650674-22-9P	650674-23-0P
	650674-24-1P	650674-25-2P	650674-26-3P	650674-27-4P	650674-28-5P
	650674-29-6P	650674-30-9P	650674-31-0P	650674-32-1P	650674-33-2P
	650674-34-3P	650674-35-4P	650674-36-5P	650674-37-6P	650674-38-7P
	650674-39-8P	650674-40-1P	650674-41-2P	650674-42-3P	650674-43-4P
	650674-44-5P	650674-45-6P	650674-46-7P	650674-47-8P	650674-48-9P
	651361-06-7P				
	RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(amino acid sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of <b>tuberculosis</b> )				
IT	7782-44-7, Oxygen, biological studies				
	RL: BSU (Biological study, unclassified); BIOL (Biological study)				
	(low; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of <b>tuberculosis</b> )				
IT	650674-49-0P	650674-50-3P	650674-51-4P	650674-52-5P	650674-53-6P
	650674-54-7P	650674-55-8P	650674-56-9P	650674-57-0P	650674-58-1P
	650674-59-2P	650674-60-5P	650674-61-6P	650674-62-7P	650674-63-8P

650674-64-9P 650674-65-0P 650674-66-1P 650674-67-2P 650674-68-3P  
 650674-69-4P 650674-70-7P 650674-71-8P 650674-72-9P 650674-73-0P  
 650674-74-1P 650674-75-2P 650674-76-3P 650674-77-4P 650674-78-5P  
 650674-79-6P 650674-80-9P 650674-81-0P 650674-82-1P 650674-83-2P  
 650674-84-3P 650674-85-4P 650674-86-5P 650674-87-6P 650674-88-7P  
 650674-89-8P 650674-90-1P 650674-91-2P 650674-92-3P 650674-93-4P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);  
 DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); PREP (Preparation); USES (Uses)

(nucleotide sequence; Mycobacterium low oxygen-induced antigens and  
 genes for vaccines or diagnostics of **tuberculosis**)

IT 650674-94-5 650674-95-6 650674-96-7 650674-97-8 650674-98-9  
 650674-99-0 650675-00-6 650675-01-7 650675-02-8 650675-03-9  
 650675-04-0 650675-05-1 650675-06-2 650675-07-3 650675-08-4  
 650675-09-5 650675-10-8 650675-11-9 650675-12-0 650675-13-1  
 650675-14-2 650675-15-3 650675-16-4 650675-17-5 650675-18-6  
 650675-19-7 650675-20-0 650675-21-1 650675-22-2 650675-23-3  
 650675-24-4 650675-25-5 650675-26-6 650675-27-7 650675-28-8  
 650675-29-9 650675-30-2 650675-31-3 650675-32-4 650675-33-5  
 650675-34-6 650675-35-7 650675-36-8 650675-37-9 650675-38-0  
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 650675-44-8 650675-45-9 650675-46-0 650675-47-1 650675-48-2  
 650675-49-3 650675-50-6 650675-51-7 650675-52-8 650675-53-9  
 650675-54-0 650675-55-1 650675-56-2 650675-57-3 650675-58-4  
 650675-59-5 650675-60-8 650675-61-9 650675-62-0 650675-63-1  
 650675-64-2 650675-65-3 650675-66-4 650675-67-5 650675-68-6  
 650675-69-7 650675-70-0 650675-71-1 650675-72-2 650675-73-3  
 650675-74-4 650675-75-5 650675-76-6 650675-77-7 650675-78-8  
 650675-79-9 650675-80-2 650675-81-3 650675-82-4 650675-83-5  
 650675-84-6 650675-85-7

RL: PRP (Properties)

(unclaimed sequence; mycobacterium low oxygen-induced antigens and  
 genes for vaccines or diagnostics o

# SYSTEM LIMITS EXCEEDED

L3 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:59568 CAPLUS  
 DN 140:127185  
 TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis**  
 diagnosis and treatment  
 IN **Andersen, Peter**; Skjot, Rikke Louise Vinther; Okkels, Li Mei  
 Meng; Brock, Inger; Oettinger, Thomas  
 PA Den.  
 SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004013685	A1	20040122	US 2001-872505	20010601
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
WO 2001004151	A2	20010118	WO 2000-DK398	20000713
WO 2001004151	A3	20010712		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	EP 1998-913536	A3	19980401		
	US 1999-289388	B2	19990412		
AB	The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and <b>RD1-ORF5</b> , from <i>Mycobacterium tuberculosis</i> . The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing <b>tuberculosis</b> caused by virulent mycobacteria in an animal, including a human being. The invention related to treating <b>tuberculosis</b> using antigens isolated from <i>Mycobacterium tuberculosis</i> .				
TI	Antigens from <i>Mycobacterium</i> as vaccine and uses in <b>tuberculosis</b> diagnosis and treatment				
IN	<b>Andersen, Peter</b> ; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas				
AB	The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and <b>RD1-ORF5</b> , from <i>Mycobacterium tuberculosis</i> . The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing <b>tuberculosis</b> caused by virulent mycobacteria in an animal, including a human being. The invention related to treating <b>tuberculosis</b> using antigens isolated from <i>Mycobacterium tuberculosis</i> .				
ST	<i>Mycobacterium</i> antigen vaccine <b>tuberculosis</b> diagnosis				
IT	Antigens RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) ( <b>RD1-ORF5</b> ; antigens from <i>Mycobacterium</i> as vaccine and uses in <b>tuberculosis</b> diagnosis and treatment)				
IT	Antigens RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (Rv2653c; antigens from <i>Mycobacterium</i> as vaccine and uses in <b>tuberculosis</b> diagnosis and treatment)				
IT	Antigens RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (Rv2654c; antigens from <i>Mycobacterium</i> as vaccine and uses in <b>tuberculosis</b> diagnosis and treatment)				
IT	<i>Mycobacterium bovis</i> (antigen <b>RD1-ORF5</b> expressed in; protein and DNA sequences of antigens from <i>Mycobacterium</i> and uses in <b>tuberculosis</b> diagnosis and treatment)				
IT	Antibodies and Immunoglobulins RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses) (antigens from <i>Mycobacterium</i> as vaccine and uses in <b>tuberculosis</b> diagnosis and treatment)				
IT	Fusion proteins (chimeric proteins) RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU				

(Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antigens in; antigens from Mycobacterium as vaccine and uses in  
**tuberculosis** diagnosis and treatment)

IT Animal  
 Human  
 (diagnosis of **tuberculosis** in; protein and DNA sequences of  
 antigens from Mycobacterium and uses in **tuberculosis**  
 diagnosis and treatment)

IT **Tuberculosis**  
 (diagnosis, **tuberculosis**; antigens from Mycobacterium as  
 vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
 (immunodiagnosis; protein and DNA sequences of antigens from  
 Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Drug delivery systems  
 (injections, intradermally; protein and DNA sequences of antigens from  
 Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Antibodies and Immunoglobulins  
 RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)  
 (monoclonal; antigens from Mycobacterium as vaccine and uses in  
**tuberculosis** diagnosis and treatment)

IT Epitopes  
 Molecular cloning  
 Mycobacterium **tuberculosis**  
**Tuberculosis**  
 Tuberculostatics  
 Vaccines  
 (protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment)

IT Immunoassay  
 (skin test; protein and DNA sequences of antigens from Mycobacterium  
 and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
 (**tuberculosis**, **tuberculosis**; antigens from  
 Mycobacterium as vaccine and uses in **tuberculosis** diagnosis  
 and treatment)

IT Immunization  
 (vaccination; protein and DNA sequences of antigens from Mycobacterium  
 and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium  
 (virulent; protein and DNA sequences of antigens from Mycobacterium and  
 uses in **tuberculosis** diagnosis and treatment)

IT Interferons  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (γ; protein and DNA sequences of antigens from Mycobacterium and  
 uses in **tuberculosis** diagnosis and treatment)

IT 649655-13-0 649655-14-1 649655-15-2 649655-16-3 649655-17-4  
 649655-18-5 649655-19-6 649655-20-9  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; antigens from Mycobacterium as vaccine  
 and uses in **tuberculosis** diagnosis and treatment)

IT 649655-09-4 649655-10-7 649655-11-8 649655-12-9  
 RL: PRP (Properties)  
 (unclaimed protein sequence; antigens from Mycobacterium as vaccine and  
 uses in **tuberculosis** diagnosis and treatment)

IT 649543-98-6 649544-02-5 649544-05-8 649544-08-1 649544-11-6  
 649544-14-9 649544-18-3 649544-21-8 649544-24-1 649544-27-4  
 649544-30-9 649544-33-2 649544-36-5 649544-40-1 649544-43-4  
 649544-46-7 649544-49-0 649544-52-5 649544-55-8 649544-58-1  
 649544-61-6 649544-65-0 649544-68-3 649544-71-8 649544-74-1  
 649544-79-6 649544-82-1 649544-85-4 649544-88-7 649544-91-2  
 649544-94-5 649544-97-8 649545-00-6 649545-03-9 649545-06-2  
 649545-09-5 649545-12-0 649545-15-3 649545-18-6 649545-21-1  
 649545-24-4 649545-27-7 649545-30-2 649545-33-5 649545-36-8  
 649545-39-1 649545-42-6 649545-45-9 649545-48-2 649545-51-7  
 649545-54-0 649545-57-3 649655-21-0 649655-22-1 649655-23-2

649655-24-3 649655-25-4 649655-26-5 649655-27-6 649655-28-7  
649655-29-8 649655-30-1

RL: PRP (Properties)

(unclaimed sequence; antigens from Mycobacterium as vaccine and uses in  
**tuberculosis** diagnosis and treatment)

L3 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment

IN **Andersen, Peter**; Weldingh, Karin; Hansen, Christina Veggerby;  
Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther;  
Rasmussen, Peter Birk

PA Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization  
of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21,  
Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/**RD1**-ORF3,  
Rv3354/CFP8A and Rv2623/TB32, from Mycobacterium **tuberculosis**.  
The invention is directed to the polypeptides and immunol. active  
fragments thereof, the genes encoding them, immunol. compns. such as  
diagnostic reagents containing the polypeptides. The invention related to  
diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by  
Mycobacterium **tuberculosis**, Mycobacterium africanum or  
Mycobacterium bovis, in an animal, including a human being. The invention  
related to treating **tuberculosis** using antigens isolated from  
Mycobacterium **tuberculosis**.

TI Protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment

IN **Andersen, Peter**; Weldingh, Karin; Hansen, Christina Veggerby;  
Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther;  
Rasmussen, Peter Birk

AB The present invention is based on the identification and characterization  
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Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/**RD1**-ORF3,  
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The invention is directed to the polypeptides and immunol. active  
fragments thereof, the genes encoding them, immunol. compns. such as  
diagnostic reagents containing the polypeptides. The invention related to  
diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by  
Mycobacterium **tuberculosis**, Mycobacterium africanum or  
Mycobacterium bovis, in an animal, including a human being. The invention  
related to treating **tuberculosis** using antigens isolated from  
Mycobacterium **tuberculosis**.

ST Mycobacterium antigen sequence **tuberculosis** diagnosis treatment

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (Ag85A, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (Ag85B, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (Ag85C, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (CFP10, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (ESAT-6, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (MPB59, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (MPB64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (MPT32, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (MPT64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (RD1-ORF2, in fusion protein; protein and DNA sequences of

antigens from Mycobacterium and uses in **tuberculosis**  
diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(RD1-ORF5, in fusion protein; protein and DNA sequences of  
antigens from Mycobacterium and uses in **tuberculosis**  
diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv0652/CFP16; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(Rv1036, in fusion protein; protein and DNA sequences of antigens from  
Mycobacterium and uses in **tuberculosis** diagnosis and  
treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv1636/TB15A; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv1984c/CFP21; protein and DNA sequences of antigens from  
Mycobacterium and uses in **tuberculosis** diagnosis and  
treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2185c/TB16; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2462c/TB51; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2623/TB32; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv3354/CFP8A; protein and DNA sequences of antigens from Mycobacterium  
and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study,

unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv3451/CFP23; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv3872/RD1-ORF3; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(TB10.4, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis

(agents, **tuberculosis**; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cell membrane

Cell wall

(antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(antigens in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cytoplasm

(cytosol, antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Animal

Human

(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium avium

Mycobacterium intracellulare

Mycobacterium marinum

Mycobacterium scrofulaceum

Mycobacterium szulgai

Mycobacterium xenopi

(expression of antigen CFP21 and CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium fortuitum

Mycobacterium kansasii

(expression of antigen CFP23 in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis

(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Lipoproteins

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

treatment)

IT Antibodies and Immunoglobulins  
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (monoclonal; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT DNA sequences  
 Epitopes  
 Immunoassay  
 Molecular cloning  
 Mycobacterium **tuberculosis**  
 Protein sequences  
**Tuberculosis**  
 Tuberculostatics  
 (protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins  
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
 (serodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium africanum  
 Mycobacterium bovis  
 Mycobacterium **tuberculosis**  
 (**tuberculosis** caused by; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium  
 (virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Crystallins  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 ( $\alpha$ -, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592558-08-2P 592558-09-3P 592558-10-6P 592558-11-7P 592558-12-8P  
 592558-13-9P 592558-14-0P 592558-15-1P 592558-16-2P, Antigen T51  
 (Mycobacterium **tuberculosis**)  
 RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (amino acid sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592557-99-8 592558-00-4 592558-01-5 592558-02-6 592558-03-7  
 592558-04-8 592558-05-9 592558-06-0 592558-07-1  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-15-4 592573-16-5 592573-17-6 592573-18-7 592573-19-8  
 592573-20-1 592573-21-2 592573-22-3 592573-23-4 592573-24-5  
 592573-26-7 592573-27-8 592573-28-9 592573-29-0 592573-30-3  
 592573-31-4 592573-32-5 592573-33-6  
 RL: PRP (Properties)

(unclaimed nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-14-3 592573-25-6

RL: PRP (Properties)

(unclaimed protein sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 213992-11-1 213992-15-5 264285-55-4 264285-57-6 264285-59-8

RL: PRP (Properties)

(unclaimed sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

L3 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:609858 CAPLUS

DN 139:163576

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

IN **Andersen, Peter**; Skjot, Rikke Louise Vinther

PA Den.

SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 1508339	A1	20050223	EP 2004-77505	19940701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
	US 5955077	A	19990921	US 1995-465640	19950605
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1999-289388	B2	19990412		
	EP 1994-919574	A3	19940701		
	EP 1998-913536	A3	19980401		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1**-ORF5,

**RD1-ORF2**, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

IN **Andersen, Peter**; Skjot, Rikke Louise Vinther

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1-ORF5**, **RD1-ORF2**, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

ST Mycobacterium **tuberculosis** antigen gene antibody vaccine  
diagnosis skin test

575506-55-7 575506-56-8 575506-57-9 575506-58-0 575506-59-1  
575506-60-4

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 575512-14-0 575512-20-8 575512-21-9 575512-22-0 575512-23-1  
575512-24-2 575512-25-3 575512-26-4 575512-27-5 575512-28-6  
575512-29-7 575512-30-0 575512-31-1 575512-32-2 575512-33-3  
575512-34-4 575512-35-5 575512-36-6 575512-37-7 575512-38-8  
575512-39-9 575512-40-2 575512-41-3 575512-43-5 575512-45-7  
575512-47-9 575512-49-1 575512-51-5 575512-53-7 575512-55-9  
575512-57-1 575512-59-3 575512-66-2 575512-67-3 575512-68-4  
575512-69-5 575512-70-8 575512-71-9 575512-72-0 575512-73-1  
575512-74-2 575512-75-3 575512-76-4 575512-77-5 575512-78-6  
575512-79-7 575512-80-0 575512-81-1 575512-82-2 575512-83-3  
575512-84-4 575512-85-5 575512-86-6 575512-87-7 575512-88-8  
575512-89-9 575512-90-2 575512-91-3 575512-92-4 575512-93-5  
575512-94-6 575512-95-7 575512-96-8 575512-97-9 575513-00-7  
575513-01-8 575513-02-9 575513-03-0 575513-04-1 575513-05-2  
575513-06-3 575513-07-4 575513-08-5 575513-10-9 575513-12-1  
575513-14-3 575513-15-4 575513-16-5 575513-17-6 575513-18-7  
575513-19-8 575513-20-1 575513-21-2 575513-22-3 575513-23-4  
575513-24-5 575513-25-6 575513-26-7 575513-27-8 575513-32-5  
575513-34-7 575513-36-9 575513-37-0 575513-39-2 575513-40-5  
575513-41-6 575513-42-7 575513-43-8 575513-44-9 575513-45-0

RL: PRP (Properties)

(unclaimed nucleotide sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 575512-15-1 575512-16-2 575512-17-3 575512-18-4 575512-19-5  
575512-42-4 575512-44-6 575512-46-8 575512-48-0 575512-50-4  
575512-52-6 575512-54-8 575512-56-0 575512-58-2 575512-60-6  
575512-61-7 575512-62-8 575512-63-9 575512-64-0 575512-65-1  
575512-98-0 575512-99-1 575513-09-6 575513-11-0 575513-13-2  
575513-29-0 575513-30-3 575513-31-4 575513-33-6 575513-35-8  
575513-38-1

RL: PRP (Properties)

(unclaimed protein sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT 213992-07-5 213992-08-6 213992-10-0 213992-11-1 213992-13-3  
213992-14-4 213992-15-5 213992-16-6 213992-17-7 213992-18-8  
213992-19-9 213992-20-2 213992-21-3 213992-23-5 213992-24-6

RL: PRP (Properties)

(unclaimed sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of

the t

SYSTEM LIMITS EXCEEDED

L3 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of Mycobacterium \*\*\*tuberculosis culture filtrates  
and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh,  
Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		
	WO 1998-DK132	W	19980401		
	EP 1998-947412	A3	19981008		
	WO 1998-DK438	W	19981008		

AB Culture filtrate antigens of Mycobacterium tuberculosis are characterized and cDNAs encoding them are cloned. Some of the proteins

are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a  $\lambda$ gt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9        THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

- TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use
- IN **Andersen, Peter**; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter
- AB Culture filtrate antigens of Mycobacterium **tuberculosis** are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a  $\lambda$ gt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.
- ST Mycobacterium culture filtrate antigen gene; vaccine **tuberculosis**  
Mycobacterium antigen gene
- IT Lipoproteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(19 kDa, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
- IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(85 complex, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
- IT Chaperonins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DnaK, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
- IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(ESAT6, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
- IT Chaperonins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(GroEL, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)
- IT Chaperonins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(GroES, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT51, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT59, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT64, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antigens  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
 (culture filtrate antigens of Mycobacterium; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**  
 (diagnosis, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Escherichia  
 Mycobacterium  
 Mycobacterium BCG  
 Pseudomonas  
 Salmonella  
 (expression host for Mycobacterium **tuberculosis** antigen genes; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Hemagglutinins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (heparin-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (monoclonal, to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium **tuberculosis**  
 (novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Molecular cloning  
 (of antigen genes of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Fusion proteins (chimeric proteins)  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(of antigens of *Mycobacterium tuberculosis*, for vaccines;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Protein sequences  
 (of antigens of *Mycobacterium tuberculosis*; novel antigens of  
*Mycobacterium tuberculosis* culture filtrates and genes  
 encoding and their diagnostic and prophylactic use)

IT DNA sequences  
 (of genes for antigens of *Mycobacterium tuberculosis*; novel  
 antigens of *Mycobacterium tuberculosis* culture filtrates and  
 genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pRVN01, expression vector for antigen genes of *Mycobacterium  
 tuberculosis* on; novel antigens of *Mycobacterium  
 tuberculosis* culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Plasmid vectors  
 (pRVN02, expression vector for antigen genes of *Mycobacterium  
 tuberculosis* on; novel antigens of *Mycobacterium  
 tuberculosis* culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT087, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT088, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT089, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT090, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT091, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT096, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
 (pT098, gene for antigen of *Mycobacterium tuberculosis* on;  
 novel antigens of *Mycobacterium tuberculosis* culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (phosphate-binding, as antigen of *Mycobacterium tuberculosis*,  
 fusion proteins containing; novel antigens of *Mycobacterium  
 tuberculosis* culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (proline-rich, as antigen of *Mycobacterium tuberculosis*,  
 fusion proteins containing; novel antigens of *Mycobacterium  
 tuberculosis* culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf2, for antigen of *Mycobacterium tuberculosis*  
 ; novel antigens of *Mycobacterium tuberculosis* culture

filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf3, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf4, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf5, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf8, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf9a, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rd1-orf9b, for antigen of Mycobacterium **tuberculosis**  
 ; novel antigens of Mycobacterium **tuberculosis** culture  
 filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (to antigens of Mycobacterium **tuberculosis**; novel antigens of  
 Mycobacterium **tuberculosis** culture filtrates and genes  
 encoding and their diagnostic and prophylactic use)

IT Mycobacterium africanum  
 Mycobacterium bovis  
 (**tuberculosis** caused by; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Diagnosis  
 (**tuberculosis**, vaccines against and diagnosis of; novel  
 antigens of Mycobacterium **tuberculosis** culture filtrates and  
 genes encoding and their diagnostic and prophylactic use)

IT Vaccines  
 (**tuberculosis**; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT **Tuberculosis**  
 (vaccines against and diagnosis of; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
 diagnostic and prophylactic use)

IT Crystallins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 ( $\alpha$ -, as antigen of Mycobacterium **tuberculosis**, fusion  
 proteins containing; novel antigens of Mycobacterium **tuberculosis**  
 culture filtrates and genes encoding and their diagnostic and  
 prophylactic use)

IT 213992-07-5 213992-08-6 213992-09-7D, amino acid-substituted analogs

213992-10-0 213992-11-1 213992-12-2 213992-13-3 213992-14-4  
213992-15-5 213992-16-6 213992-17-7 213992-18-8 213992-19-9  
213992-20-2 213992-21-3 213992-22-4 213992-23-5 213992-24-6  
214072-43-2 214072-44-3 214072-45-4 214072-46-5 214072-47-6  
214142-58-2

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(N-terminal peptide of Mycobacterium **tuberculosis** antigen;  
novel antigens of Mycobacterium **tuberculosis** culture  
filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium BCG strain Tokyo ribosome)  
208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7  
208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9  
208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6  
208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9  
208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4  
214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3  
214349-26-5 214349-38-9

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, Glutamine synthetase,  
fusion products 9029-06-5D, Alanine dehydrogenase, fusion products  
9054-89-1D, Superoxide dismutase, fusion products

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(as antigen of Mycobacterium **tuberculosis**; novel antigens of  
Mycobacterium **tuberculosis** culture filtrates and genes  
encoding and their diagnostic and prophylactic use)

IT 214348-46-6 214348-59-1 214348-61-5 214348-62-6 214348-68-2  
214348-69-3 214348-70-6 214348-76-2 214348-77-3 214348-79-5  
214348-80-8 214348-81-9 214348-82-0 214348-83-1 214348-85-3  
214348-86-4 214348-88-6 214348-89-7 214348-90-0 214348-91-1  
214348-93-3 214349-11-8 214349-21-0 214349-23-2 214349-25-4  
214349-28-7 214349-47-0 214349-53-8 214349-54-9 214349-57-2  
214349-60-7 214349-62-9 214349-63-0

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleotide sequence; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)

L3 ANSWER 12 OF 14 MEDLINE on STN

AN 2005184291 IN-PROCESS

DN PubMed ID: 15817755

TI Prospective evaluation of a whole-blood test using Mycobacterium  
**tuberculosis**-specific antigens ESAT-6 and CFP-10 for diagnosis of  
active **tuberculosis**.

AU Ravn Pernille; Munk Martin E; Andersen Ase B; Lundgren Bettina; Lundgren  
Jens D; Nielsen Lars N; Kok-Jensen Axel; **Andersen Peter**;  
Weldingh Karin

CS Department of Infectious Diseases, Hvidovre Hospital, Kettegards Alle 30,  
2650 Hvidovre, Copenhagen, Denmark.. pravn@dadlnet.dk

SO Clinical and diagnostic laboratory immunology, (2005 Apr) 12 (4) 491-6.  
Journal code: 9421292. ISSN: 1071-412X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals

ED Entered STN: 20050409

Last Updated on STN: 20050511

AB A new immunodiagnostic test based on the Mycobacterium  
**tuberculosis**-specific antigens CFP-10/ESAT-6(QFT-RD1)  
has been launched as an aid in the diagnosis of latent  
**tuberculosis** (TB) infection (LTBI). The aim of this study was to  
evaluate this test for the diagnosis of active TB. Eighty-two patients

with suspicion of TB and 39 healthy BCG-vaccinated persons were enrolled. Forty-eight had active TB, 25 did not, and 9 were excluded. Sensitivity and specificity of the test for active TB were evaluated in a prospective blinded manner in patients suspected of TB. The sensitivity of the QFT-RD1 was 85% (40/48; confidence interval [CI], 75 to 96), and it was higher than the sensitivity of microscopy, 42% (20/48; CI, 27 to 56; P = 0.001), and culture, 59% (27/46; CI, 44 to 73; P = 0.009). Of patients with extrapulmonary TB, 92% (12/13) were QFT-RD1 positive, whereas only 31% (4/13) were positive by microscopy and 42% (5/12) by culture (P < 0.05), and 87% (13/15) of those who were negative by both microscopy and culture were QFT-RD1 positive. By combining microscopy and culture with the QFT-RD1 test, sensitivity increased to 96% (CI, 90 to 102). Ten of 25 (40%) non-TB patients were QFT-RD1 positive, resulting in a specificity of 60%. However, 80% (8/10) of these had risk-factors for TB, indicating latent infection in this group. In healthy controls, only 3% (1/39) were QFT-RD1 positive. In conclusion, the QFT-RD1 test is sensitive for diagnosis of TB, especially in patients with negative microscopy and culture. The accuracy of the QFT-RD1 test will vary with the prevalence of LTBI. We suggest that the QFT-RD1 test could be a very useful supplementary tool for the diagnosis of TB.

TI Prospective evaluation of a whole-blood test using Mycobacterium tuberculosis-specific antigens ESAT-6 and CFP-10 for diagnosis of active tuberculosis.

AU Ravn Pernille; Munk Martin E; Andersen Ase B; Lundgren Bettina; Lundgren Jens D; Nielsen Lars N; Kok-Jensen Axel; Andersen Peter; Weldingh Karin

AB A new immunodiagnostic test based on the Mycobacterium tuberculosis-specific antigens CFP-10/ESAT-6 (QFT-RD1) has been launched as an aid in the diagnosis of latent tuberculosis (TB) infection (LTBI). The aim of this study was to evaluate this test for the diagnosis of active TB. Eighty-two test for active TB were evaluated in a prospective blinded manner in patients suspected of TB. The sensitivity of the QFT-RD1 was 85% (40/48; confidence interval [CI], 75 to 96), and it was higher than the sensitivity of microscopy, 42% (20/48; P = 0.001), and culture, 59% (27/46; CI, 44 to 73; P = 0.009). Of patients with extrapulmonary TB, 92% (12/13) were QFT-RD1 positive, whereas only 31% (4/13) were positive by microscopy and 42% (5/12) by culture (P < 0.05), and 87% (13/15) of those who were negative by both microscopy and culture were QFT-RD1 positive. By combining microscopy and culture with the QFT-RD1 test, sensitivity increased to 96% (CI, 90 to 102). Ten of 25 (40%) non-TB patients were QFT-RD1 positive, resulting in a specificity of 60%. However, 80% (8/10) of these had risk-factors for TB, indicating latent infection in this group. In healthy controls, only 3% (1/39) were QFT-RD1 positive. In conclusion, the QFT-RD1 test is sensitive for diagnosis of TB, especially in patients with negative microscopy and culture. The accuracy of the QFT-RD1 test will vary with the prevalence of LTBI. We suggest that the QFT-RD1 test could be a very useful supplementary tool for the diagnosis of TB.

L3 ANSWER 13 OF 14 USPATFULL on STN

AN 2004:76186 USPATFULL

TI Therapeutic TB vaccine

IN Andersen, Peter, Bronshoj, DENMARK  
Rosenkrands, Ida, Vaerloose, DENMARK  
Stryhn, Anette, Virum, DENMARK

PI US 2004057963 A1 20040325

AI US 2003-617038 A1 20030711 (10)

PRAI DK 2002-1098 20020713  
US 2002-401725P 20020807 (60)

DT Utility

FS APPLICATION

LREP HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321  
NORRISTOWN ROAD, SPRING HOUSE, PA, 19477

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Therapeutic vaccines comprising polypeptides expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**

IN Andersen, Peter, Bronshoj, DENMARK

AB . . . . . expressed during the latent stage of mycobacteria infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**.

SUMM [0002] The present invention discloses a therapeutic vaccine against latent or active **tuberculosis** infection caused by the **tuberculosis** complex microorganisms (Mycobacterium **tuberculosis**, M.bovis, M.africanum). The invention furthermore discloses a multi-phase vaccine that can be administered either prophylactically or therapeutically as well as a diagnostic reagent for the detection of latent stages of **tuberculosis**.

SUMM [0003] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent decades this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM [0004] Organisms of the **tuberculosis** complex can cause a variety of diseases, but the commonest route of invasion is by inhalation of bacteria. This initiates. . . . . for the rest of their life. Certainly, individuals who have been healthy for years or even decades can suddenly develop **tuberculosis**, which has proven to be caused by the same organism they were infected with many years previously. M. **tuberculosis** and other organisms of the TB complex are unique in that the mycobacteria can evade the immune response and survive.

SUMM [0005] The course of a M. **tuberculosis** infection runs essentially through 3 phases, as illustrated in FIG. 1. During the acute phase, the bacteria proliferate in the. . . . . a latent phase is established where the bacterial load is kept stable at a low level. In this phase M. **tuberculosis** goes from active multiplication to dormancy, essentially becoming non-replicating and remaining inside the granuloma. In some cases, the infection goes. . . . .

SUMM [0009] It has been suggested that the transition of M. **tuberculosis** from primary infection to latency is accompanied by changes in gene expression (see, for example, Honer zu Bentrup, 2001, which. . . . .

SUMM . . . . . candidate. The only way to determine if a protein is recognized by the immune system during latent infection with M. **tuberculosis** is to produce the given protein and test it in an appropriate assay as described herein. Of the more than. . . . .

DRWD . . . . . the infection. For analysis of therapeutic vaccinations a reactivation model is established, where aerosol infected mice are treated with anti-M **tuberculosis** drugs for 8 weeks from the peak of infection (6 weeks after infection). This induces a latent infection phase with. . . . .

DRWD . . . . . In FIG. 2A, the immunization was given as a prophylactic vaccine 6 weeks before the mice were given a M. **tuberculosis** infection (approx. 250 bacilli) through the aerosol route with. Bacterial numbers in the lung was enumerated 6 weeks post infection.. . . .

DETD [0024] The invention is related to preventing, treating and detecting infections caused by species of the **tuberculosis** complex (Mycobacterium **tuberculosis**, M. bovis, M. africanum) by the use of a polypeptide comprising a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof, or by the use of a DNA sequence encoding a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof. The invention discloses a new therapeutic vaccine against **tuberculosis** comprising antigens

induced during the latent stage of TB-infection. It also discloses a multiphase vaccine incorporating a combination of prophylactic and therapeutic antigens as well as diagnostic reagents for the detection of the latent stage of *M. tuberculosis* infection.

DETD . . . mycobacteria infection, which stage is characterized by low-oxygen tension in the microenvironment of the mycobacteria, for a therapeutic vaccine against **tuberculosis**.

DETD . . . with efficacy as prophylactic vaccines, where the fusion partner is selected from e.g. the group consisting of ESAT-6, TB10.4, CFP10, **RD1-ORF5**, **RD1-ORF2**, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

DETD [0033] The invention further discloses a therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection.

DETD [0036] The invention also discloses a method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the above-mentioned vaccine.

DETD [0037] The invention also discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the above mentioned vaccine.

DETD . . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being.

DETD . . . use of a nucleic acid fragment according to the invention for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, and the use of a nucleic acid fragment according to the invention for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

DETD . . . a still further embodiment, the invention discloses a vaccine for immunizing an human being or other mammal or animal, against **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a . . .

DETD [0049] (b) isolating the polypeptide from a whole mycobacterium, e.g. *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, from culture filtrate or from lysates or fractions thereof; or

DETD [0051] The invention also discloses a method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . immunogenic composition as defined above, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis**

DETD [0052] In another embodiment, the invention discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the polypeptide as defined above, the immunogenic composition according to.

DETD . . . detecting binding of a antibody to said polypeptide, said binding being an indication that said subject is infected by

Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

DETD [0082] A preferred polypeptide within the present invention is an immunogenic antigen from M. **tuberculosis** produced when the organism is subjected to the stresses associated with latent infection. Such antigen can for example also be derived from the M. **tuberculosis** cell and/or M. **tuberculosis** culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native M. **tuberculosis** antigen or be heterologous and such sequences may, but need not, be immunogenic.

DETD . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in.

DETD [0085] By the term "virulent mycobacterium" is understood a bacterium capable of causing the **tuberculosis** disease in an animal or in a human being. Examples of virulent mycobacteria include but are not limited to M. **tuberculosis**, M. africanum, and M. bovis. Examples of relevant animals are cattle, possums, badgers and kangaroos.

DETD [0088] By "a latently infected individual" is understood an individual, who has been infected by a virulent mycobacterium, e.g. M. **tuberculosis**, but shows no sign of active **tuberculosis**. It is likely that individuals who have been vaccinated, e.g. by BCG, or treated for TB may still retain the. . . for PPD reactivity. Nonetheless, in its most accurate sense, "latently-infected" may be used to describe any individual who has M. **tuberculosis** residing in their tissues but who is not clinically ill.

DETD [0101] In the context of providing candidate molecules for a new vaccine against **tuberculosis**, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been shown (Olsen, 2000) that.

DETD . . . response may also be determined by the use of T cell lines derived from an immune individual or an M. **tuberculosis** -infected person where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture. . .

DETD [0114] In general, M. **tuberculosis** antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures.

DETD [0115] They may be purified as native proteins from the M. **tuberculosis** cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a.

DETD . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from M. **tuberculosis**, such as of a polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystalline, or at least one T-cell epitope. . .

DETD . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

DETD . . . from M. leprae. Antigens with therapeutic properties may be identified based on their ability to diminish the severity of M. **tuberculosis** infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic. . .

DETD [0161] Cloning and Expression of Low Oxygen Induced M. **tuberculosis** Antigens in E. coli.

DETD [0162] A number of M **tuberculosis** genes are induced under low oxygen conditions. The upregulation of the genes listed in table 2 has been determined at.

DETD . . . Ammonium Sulfate, 0.2 mM of each of the four nucleotides, 0.2  $\mu$ M of each primer and 10 ng of M. **tuberculosis** H37Rv

chromosomal DNA. The reaction mixtures were initially heated to 95° C. for 5 min., followed by 35 cycles of: . . .

DETD . . . with recombinant antigens. Six weeks after the last immunization, the mice are given an aerosol infection with approximately 250 M. **tuberculosis** bacilli. The protective capacity of the vaccine is evaluated by enumeration of the bacteria in spleen and lung 6 weeks. . . .

DETD . . . reactivation model of latent TB has been established (van Pinxteren, 2000) (FIG. 1B). An aerosol infection with approximately 250 M. **tuberculosis** bacilli is given and at the peak of infection 6 weeks later, the mice receive an 8-week course of anti-mycobacterial. . . .

DETD . . . cells is significantly higher in the unimmunized group. ESAT6 is an antigen produced in high amounts by the actively-growing M. **tuberculosis** bacteria. The level of the ESAT6 specific immune response in infected mice could therefore be indicative the degree of actively-growing. . . . have in fact demonstrated such a correlation between the level of ESAT6 response and degree of disease in both M. **tuberculosis**-infected humans and M. bovis-infected cattle (Doherty, 2002, Vordermeier, 2002). Therefore, the higher ESAT6 response in the unimmunized group of latently-infected. . . .

DETD . . . lungs of the Rv0569 vaccinated mice, whereas neither ESAT6 nor BCG are able to inhibit the growth of the M. **tuberculosis** bacteria when given as a vaccine during latent infection. That is, the induction of Rv0569 T cell responses can participate. . . .

DETD [0182] Anon. 2001. Global **Tuberculosis** Control. WHO Report.

DETD [0202] Danish Patent application PA 2000 00666 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0203] Danish Patent application PA 1999 01020 (WO 01/23388) " **Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD [0204] Patent application U.S. Ser. No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis** "

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 273

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

Val Glu Pro Lys Arg Ser Arg Leu Val Val Cys Ala Pro Glu Pro Ser

1 5 10. . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 152

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 2

Met Ser Pro Gly Ser Arg Arg Ala Ser Pro Gln Ser Ala Arg Glu Val

1 5 10. . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 3

LENGTH: 114

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 3

Val Glu Ser Glu Pro Leu Tyr Lys Leu Lys Ala Glu Phe Phe Lys Thr

1 5 10. . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 4

LENGTH: 344

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 4

Met Pro Ile Ala Thr Pro Glu Val Tyr Ala Glu Met Leu Gly Gln Ala

1 5 10. . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 5

LENGTH: 113  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 5  
 Met Gly Glu His Ala Ile Lys Arg His Met Arg Gln Arg Lys Pro Thr  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 6  
 LENGTH: 380  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 6  
 Val Ala Gly Asn Pro Asp Val Val Thr Val Leu Leu Gly Gly Asp Val  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 7  
 LENGTH: 397  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 7  
 Val Thr Asp His Val Arg Glu Ala Asp Asp Ala Asn Ile Asp Asp Leu  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 8  
 LENGTH: 446  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 8  
 Met Val Glu Pro Gly Asn Leu Ala Gly Ala Thr Gly Ala Glu Trp Ile  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 9  
 LENGTH: 210  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 9  
 Met Ile Ala Thr Thr Arg Asp Arg Glu Gly Ala Thr Met Ile Thr Phe  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 10  
 LENGTH: 80  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 10  
 Met Thr Asn Val Gly Asp Gln Gly Val Asp Ala Val Phe Gly Val Ile  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 11  
 LENGTH: 652  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 11  
 Val Thr Val Thr Pro Arg Thr Gly Ser Arg Ile Glu Glu Leu Leu Ala  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 12  
 LENGTH: 395  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 12  
 Met Arg Gly Gln Ala Ala Asn Leu Val Leu Ala Thr Trp Ile Ser Val  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 13  
 LENGTH: 94  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 13

Met Cys Gly Asp Gln Ser Asp His Val Leu Gln His Trp Thr Val Asp  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 14  
 LENGTH: 560  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 14  
 Met Ile Pro Thr Met Thr Ser Ala Gly Trp Ala Pro Gly Val Val Gln  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 15  
 LENGTH: 143  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 15  
 Met Ile Thr Asn Leu Arg Arg Arg Thr Ala Met Ala Ala Gly Leu  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 16  
 LENGTH: 905  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 16  
 Leu Ser Ala Ser Val Ser Ala Thr Thr Ala His His Gly Leu Pro Ala  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 17  
 LENGTH: 258  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 17  
 Met Ser Phe His Asp Leu His His Gln Gly Val Pro Phe Val Leu Pro  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 18  
 LENGTH: 285  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 18  
 Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 19  
 LENGTH: 285  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 19  
 Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 20  
 LENGTH: 114  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 20  
 Val Thr Tyr Val Ile Gly Ser Glu Cys Val Asp Val Met Asp Lys Ser  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 21  
 LENGTH: 279  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 21  
 Met Asn Gln Ser His Lys Pro Pro Ser Ile Val Val Gly Ile Asp Gly  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 22

LENGTH: 339  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 22  
 Met Thr Glu Pro Ala Ala Trp Asp Glu Gly Lys Pro Arg Ile Ile Thr  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 23  
 LENGTH: 681  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 23  
 Val Leu Met Thr Ala Ala Ala Asp Val Thr Arg Arg Ser Pro Arg Arg  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 24  
 LENGTH: 144  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 24  
 Met Ala Thr Thr Leu Pro Val Gln Arg His Pro Arg Ser Leu Phe Pro  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 25  
 LENGTH: 331  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 25  
 Met Pro Asp Thr Met Val Thr Thr Asp Val Ile Lys Ser Ala Val Gln  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 26  
 LENGTH: 195  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 26  
 Met Pro Leu Leu Thr Ile Gly Asp Gln Phe Pro Ala Tyr Gln Leu Thr  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 27  
 LENGTH: 272  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 27  
 Met Ser Gly Arg Gly Glu Pro Thr Met Lys Thr Ile Ile Val Gly Ile  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 28  
 LENGTH: 393  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 28  
 Met Arg Asp Ala Ile Pro Leu Gly Arg Ile Ala Gly Phe Val Val Asn  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 29  
 LENGTH: 413  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 29  
 Met Ala Ser Ser Ala Ser Asp Gly Thr His Glu Arg Ser Ala Phe Arg  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 30  
 LENGTH: 120  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 30

Met Ser Thr Gln Arg Pro Arg His Ser Gly Ile Arg Ala Val Gly Pro  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 31  
LENGTH: 374  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 31  
Met Arg Ser Glu Arg Leu Arg Trp Leu Val Ala Ala Glu Gly Pro Phe  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 32  
LENGTH: 179  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 32  
Met Leu His Arg Asp Asp His Ile Asn Pro Pro Arg Pro Arg Gly Leu  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 33  
LENGTH: 375  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 33  
Val Thr Gln Thr Gly Lys Arg Gln Arg Arg Lys Phe Gly Arg Ile Arg  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 34  
LENGTH: 371  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 34  
Met Arg Val Gly Ile Pro Thr Glu Thr Lys Asn Asn Glu Phe Arg Val  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 35  
LENGTH: 104  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 35  
Met Val Ile Arg Phe Asp Gln Ile Gly Ser Leu Val Leu Ser Met Lys  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 36  
LENGTH: 344  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 36  
Val Leu Lys Asn Ala Val Leu Leu Ala Cys Arg Ala Pro Ser Val His  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 37  
LENGTH: 336  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 37  
Val Trp Ser Ala Ser Gly Gly Gln Cys Gly Lys Tyr Leu Ala Ala Ser  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 38  
LENGTH: 110  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 38  
Val Val Gln Gly Arg Thr Val Leu Phe Arg Thr Ala Glu Gly Ala Lys  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 39

LENGTH: 463  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 39  
Met Asn His Leu Thr Thr Leu Asp Ala Gly Phe Leu Lys Ala Glu Asp  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 40

LENGTH: 332

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 40

Met Asn Thr His Phe Pro Asp Ala Glu Thr Val Arg Thr Val Leu Thr  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 41

LENGTH: 578

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 41

Met Thr Thr Gly Gly Leu Val Asp Glu Asn Asp Gly Ala Ala Met Arg  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 42

LENGTH: 268

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 42

Met Ser Asp Pro Arg Pro Ala Arg Ala Val Val Val Gly Ile Asp Gly  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 43

LENGTH: 181

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 43

Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 44

LENGTH: 274

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 44

Met Thr Trp Ala Asp Glu Val Leu Ala Gly His Pro Phe Val Val Ala  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 45

LENGTH: 248

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 45

Val Ser Asp Gly Glu Gln Ala Lys Ser Arg Arg Arg Arg Gly Arg Arg  
1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 46

LENGTH: 819

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 46

gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60  
ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120  
gctcgtgccg tgggtcgcgt gttggccgat cggggcgta ccgggggtgc. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 47

LENGTH: 819

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 47  
 gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60  
 ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacgggtg 120  
 gctcgtgccg tgggtcgcgt gttggccgat cggggcgta cggggggtgc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 48  
 LENGTH: 342  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 48  
 gtggagtccg aaccgctgta caagctcaag gcggagtctt tcaaaaccct tgcgcatccg 60  
 gcgcggatca ggattttgga gctgctggtc gagcgggacc gttcggtcgg tgagttgctg 120  
 tcctcggacg tcggcctgga gtcgtcgaac ctgtcccagc agctgggtgt. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 49  
 LENGTH: 1032  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 49  
 atgcctatcg caacgcccga ggtctacgcg gagatgctcg gtcaggccaa acaaaactcg 60  
 tacgctttcc cggctatcaa ctgcacctcc tcggaaaccg tcaacgccgc gatcaaagg 120  
 ttcgccgacg ccggcagtga cggaatcatc cagttctcga ccggtggcgc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 50  
 LENGTH: 339  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 50  
 atgggtgagc acgccatcaa gcggcacatg cggcaacgga agcctacgaa gcatcccccta 60  
 gccagaaaac ggggcgcgcg gattctggtc ttaccgacg atccccgcag gagcgctctc 120  
 atagtgcccg gttgccacct ggattccatg cgccgagaaa agaacgcgta. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 51  
 LENGTH: 1140  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 51  
 gtggctggca atcctgatgt ggtgacggtg ctgctgggcg gtgacgtcat gctcggccgt 60  
 ggcgtcgatc agatcctgcc tcatcccgcc aaaccgcaat tgcgcgaacg gtatatgcgg 120  
 gatgcgaccg gctatgttcg cctggccgag cgggtgaacg ggcgcattcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 52  
 LENGTH: 1191  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 52  
 gtgacagacc acgtgcgcga ggcggacgac gcgaacatcg acgatctgtt gggcgacctg 60  
 ggcggatacc cgcgcgcga gctgcggaag ctgtgcgagt ggttgctcga gcagggcatc 120  
 acccccgacg agattcgggc gaccaaccg ccgttgctgc tggccacccg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 53  
 LENGTH: 1338  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 53  
 atggtagagc ccggcaattt ggcaggcgcg accggcgccg aatggatcgg ccggccaccg 60  
 cacgaggaat tgcagcgcaa agtgcgcccg ctgctgccat ccgacgatcc gttctacttc 120  
 ccacctgccc gctaccagca tgccgtgccc ggaacggtgt tgcgctcgcg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 54  
 LENGTH: 630  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 54  
 atgatcgcca caaccgcga tcgtgaagga gccaccatga tcacgtttag gctgcgcttg 60  
 ccgtgccgga cgatactgcg ggtgttcagc cgcaatccgc tgggtgcgtg gacggatcga 120  
 ctcgaggcgg tcgtcatgct gctggccgtc acggtctcgc tgctgactat. . .  
 DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 55  
 LENGTH: 240  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 55  
 atgaccaacg tcggtgacca ggggggttgac gcggtcttcg ggggtgatcta cccacctcag 60  
 gtcgcgctgg tcagtttcgg caagccggca caacgagttt gcgccgtcga cggcgcgac 120  
 cacgtcatga cgaccgtgct ggctacgctg cccgctgacc acggctgcag.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 56  
 LENGTH: 1956  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 56  
 gtgacgggta caccacggac cggcagccgc atcgaggagc tgcttgacg cagcggccgg 60  
 ttcttcatcc cgggtgagat ctccggcgat ctgcgtaccg tgaccgcgc cggcggccgc 120  
 gacggcgacg tgttctatcg agaccgggtg agccacgaca aggtggtccg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 57  
 LENGTH: 1185  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 57  
 atgagagggc aagcggccaa tctcgtgctg gccacctgga tctcggtggt caacttctgg 60  
 gcgtggaacc tgatcggccc gctgtcgacc agctacgcgc gtgacatgtc actgtccagc 120  
 gccgaggcgt cgctgctcgt cgccaccccg atcctggtgg gtgcccttgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 58  
 LENGTH: 282  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 58  
 atgtgcggcg accagtcgga tcacgtgctg cagcactgga ccgtcgacat atcgatcgac 60  
 gaacacgaag gattgactcg ggcgaaggca cggctgcgtt ggcgggaaaa ggaattggtg 120  
 ggtgttgggc tggcaaggct caatccggcc gaccgcaacg tccccgagat.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 59  
 LENGTH: 1680  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 59  
 atgattccca cgatgacatc ggccggctgg gcaccagggg tgggtgcagtt ccgcgaatac 60  
 caacggcggt ggctgcgcgg cgatgtcctc gccggcctga ccgtggccgc ctatctgac 120  
 ccgcaagcga tggcgtatgc gaccgtggcg ggcctaccgc cggcagccgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 60  
 LENGTH: 429  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 60  
 atgatcacia acctccgacg ccgaaccgcg atggcagccg ccggcctagg ggctgctctc 60  
 gggctgggca tcctgctggg tccgacggtg gacgcccac tcgccaacgg ttcgatgtcg 120  
 gaagtcatga tgtcggaaat tgccgggttg cctatccctc cgattatcca.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 61  
 LENGTH: 2715  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 61  
 ttgtcggcgt cagtgtctgc cacgacggct catcatggct tgccagcaca tgaagtgggtg 60  
 ctgctgctgg agagcgatcc atatcacggg ctgtccgacg gcgaggccgc ccaacgacta 120  
 gaacgcttcg ggcccaacac cttggcggtg gtaacgcgcg ctagcttgct.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 62  
 LENGTH: 774  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 62

atgagtttcc acgatcttca tcaccaaggt gttccgttcg tgttgcccaa cgcctgggat 60  
 gtgccgtcgg ccctggccta cctcgcggag ggcttcacgg ctatcggcac aaccagtttc 120  
 ggggtctcgt ccagcggcgg gcacccggac gggcaccgcg ccaactcgcgg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 63  
 LENGTH: 855  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 63  
 gtggtcaagc gctctcgggc aacccgactt tcgccgagca tctggtccgg atgggaatca 60  
 cctcagtgtc ggtccattcg ggcgcgattg ctgctacccc ggggtcggtc gcggccgccc 120  
 aacgccgatt gttgctggaa tcagctcgcg gtgacgcctg acacccggat. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 64  
 LENGTH: 885  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 64  
 atgtctaaac cccgcaagca gcacggagtt gtcgtcgggg tagatggttc gctcgaatcg 60  
 gatgccgccc cctgttgggg tgccaccgat gcggcgatga ggaacattcc gctgaccgtg 120  
 gtccacgtgg tgaacgccga tgtagcgacg tggccgccga tgccgtatcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 65  
 LENGTH: 342  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 65  
 gtgacctatg tgatcggtag tgagtgcgtg gatgtgatgg acaagtcctg tgtgcaggag 60  
 tgtccggctc actgtatcta tgagggcgcc cgaatgctct acatcaaccc cgacgagtgc 120  
 gtggattgtg gtgcgtgcaa accggcctgc cgcgtcgagg cgatctactg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 66  
 LENGTH: 837  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 66  
 atgaaccaat cacacaaacc cccatcgatc gtcgtcggta ttgatggctc gaagccggcc 60  
 gtgcaagccc cactgtgggc ggtcgacgag gcagccagcc gtgacatccc gctgcgtctg 120  
 ctgtacgcga tcgaaccca cgatcccggg tacgccgcac acggcgcgcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 67  
 LENGTH: 1017  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 67  
 atgacggagc cagcggcgtg ggacgaaggc aagccgcgaa tcatcacttt gaccatgaac 60  
 cccgccttgg acatcacgac gagcgtcgac gtggtgcgcc cgaccgagaa aatgcgttgt 120  
 ggcgcacctc gctacgatcc cggcggcgcc ggtatcaatg tcgcccgcac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 68  
 LENGTH: 2043  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 68  
 gtgctgatga ccgcagcggc tgatgtcacc cggcgctcgc cgcggcgcgt gttccgtgac 60  
 cgccgcgagg ccggccgggt gctggcggaa ttactcgccc cctatcggga ccagccggac 120  
 gtgattgtgc tcggcttggc ccggggtggc ctcccggtcg catgggaggt. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 69  
 LENGTH: 432  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 69  
 atggccacca cccttcccgt tcagcgccac ccgcgggtccc tcttccccga gttttctgag 60  
 ctgttcgcgg ccttcccgtc attcgccgga ctccggccca ccttcgacac ccggttgatg 120  
 cggctggaag acgagatgaa agaggggccc tacgaggtac gcgcggagct. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 70

LENGTH: 993  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 70  
 atgccggaca ccatgggtgac caccgatgtc atcaagagcg cgggtgcagtt ggcctgccgc 60  
 gcaccgtcgc tccacaacag ccagccctgg cgctggatag ccgaggacca cacggttgcg 120  
 ctggttcctcg acaaggatcg ggtgctttac gcgaccgacc actccggccg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 71  
 LENGTH: 585  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 71  
 atgccactgc taaccattgg cgatcaattc cccgcctacc agctcaccgc tctcatcggc 60  
 ggtgacctgt ccaaggctga cgccaagcag cccggcgact acttcaccac tatcaccagt 120  
 gacgaacacc caggcaagtg gcgggtggtg ttcttttggc cgaaagactt.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 72  
 LENGTH: 816  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 72  
 atgtctggga gaggagagcc gacgatgaaa acaatcattg ttggtatcga tggttcgcac 60  
 gcggcgatta cggccgcatt gtgggggggtt gacgaggcca tcagccgagc ggtgccgctg 120  
 cgactggtct cagtgatcaa gccgacacat ccgtccccgg acgactacga.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 73  
 LENGTH: 1179  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 73  
 atgcgtgatg cgatcccgtt tgggcggatc gccgggtttg tggatgaacgt ccactggagc 60  
 gtgttggtga tctgtgggtt gttcacctgg agtctggcga ccatgttgcc gggtagcgtc 120  
 ggaggctacc cggccgtggt ctattggctt ctcggcgcag gtggcgcggt.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 74  
 LENGTH: 1239  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 74  
 atggcaagtt ctgcgagcga cggcaccac gaacgctcgg cttttcgcct gagtccaccg 60  
 gtcttgagcg gcgcatggg accgttcacg cacaccggtc tgtacgtcgc tcaatcgtgg 120  
 cgcgactatc tgggtcaaca gcccataaa ctgccgatcg cacggccac.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 75  
 LENGTH: 360  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 75  
 atgtccacgc aacgaccgag gcactccggt attcgggctg ttggccccta cgcattgggc 60  
 ggccgatgtg gtcgatagg cagggtgggg gtgcaccagg aggcgatgat gaatctagcg 120  
 atatggcacc cgcgaagggt gcaatccgcc accatctatc aggtgaccga.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 76  
 LENGTH: 1122  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 76  
 atgcgatcag aacgtctccg gtggctggta gccgcagaag gtccgttcgc ctcggtgtat 60  
 ttcgacgact cgcacgacac tcttgatgcc gtcgagcgcc gggaaagcgac gtggcgcgat 120  
 gtccggaagc atctcgaaag ccgcgacgcg aagcaggagc tcatcgacag.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 77  
 LENGTH: 537  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 77  
 atgctgcacc gcgacgatca catcaatccg ccgcggcccc gcgggttggg tggttccttg 60

gccgcctac gāgcgacaaa tcccctgcgc gccttggcgc gttgcgttca ggcgggcaag 120  
 ccgggcacca gttaaggga tccgtccgtg ccgcatacgg cggacttgcg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 78  
 LENGTH: 1125  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 78  
 gtgacgcaaa ccggcaagcg tcagagacgc aaattcgggtc gcatccgaca gttcaactcc 60  
 ggccgctggc aagccagcta caccggcccc gacggccgcg tgtacatcgc ccccaaaaacc 120  
 ttcaacgcca agatcgacgc cgaagcatgg ctcaccgacc gccgcccgcga. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 79  
 LENGTH: 1113  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 79  
 atgcgcgtcg gtattccgac cgagacaaa aacaacgaat tccgggtggc catcaccccc 60  
 gccggcgctcg cggaaactaac ccgtcgtggc catgaggtgc tcatccaggc aggtgccgga 120  
 gagggtcgcg ctatcaccga cgcggatttc aaggcggcag gcgcgcaact. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 80  
 LENGTH: 312  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 80  
 atggtcatcc ggtttgatca aataggggtc ttggctctct caatgaaatc ccttgcgta 60  
 ctgtcgtttc agcgggtgtc gcgcgagaat tctagtttgg tcgcggcgct ggaccggctc 120  
 gatgctgcgg tcgatgagct gacgcctttg tcgtttgatg cgttgaccac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 81  
 LENGTH: 1032  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 81  
 gtgctcaaga acgcagtctt gctggcatgc cgggcgccgt cggtgacaaa cagccagccc 60  
 tggcgttggg tggccgaaa cggctccgag cacactactg tgcaacctgt cgtcaaccgc 120  
 caccgaacgg tgccggccac cgaccattcc ggccggcaag cgatcatcag. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 82  
 LENGTH: 1011  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 82  
 gtgtggtccg cctcgggtgg gcagtgcggg aagtatcttg ccgcctcgat ggtgctgcag 60  
 cttgatgggt tggaaagtca cgggtgtgtg gagtttggg gtgaccgcta tggccccgag 120  
 gtgcgtgagg agctgttggc gatgagtgcg gccagcatcg atcgttatct. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 83  
 LENGTH: 330  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 83  
 gtggtgcaag gccgcaccgt gctgtttcgt accgcggagg gcgcgcaaatt attttcagcc 60  
 gtgcgaaagt gcgcggtggc tttcgaggcg gacgaccaca acgttgccga gggctggagc 120  
 gtgatcgtca aggttcgcgc ccagggtgctg acgaccgacg cgggggtccg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 84  
 LENGTH: 1389  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 84  
 atgaatcacc taacgacact tgacgccggg tttctcaagg cagaagacgt ggatcggcac 60  
 gtgagtctgg caatcggcgc tctggcggtc atcgaggggc cggctcccga tcaggaagcc 120  
 ttcttatcgt cgctcgctca acgcctacgt ccctgtaccc ggttcgggca. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 85  
 LENGTH: 996

TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 85  
 atgaacaccc atttcccga cgccgaaacc gtgcgaacgg ttctcaccct ggccgtccgg 60  
 gccccctcca tccacaacac gcagccgtgg cgggtggcggg tatgcccga gagtctggag 120  
 ctgttctcta gacccgatat gcagctgcgt agcaccgatc cggacgggcg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 86  
 LENGTH: 1734  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 86  
 atgacaacag ggggcctcgt cgacgaaaac gacggcgccg caatgcgtcc actgcgtcac 60  
 acgctctccc aactacgcct gcacgagctg ctgggtcgagg tgcaggaccg ggtcgagcag 120  
 atcgtcgagg gccgggaccg cctcgatggt ctgggtggagg ccatgctcgt.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 87  
 LENGTH: 804  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 87  
 atgagcgtac ctccggccagc tcgggcagtg gtcgttggtg tcgacgggtc aagggcggca 60  
 acgcatgcgg cgttggtggc ggtcgatgag gcggtgaacc gagacattcc gctgcgactg 120  
 gtgtacgtca tcgatccgtc ccaactgtcc gccgccggcg agggcggtgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 88  
 LENGTH: 543  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 88  
 atgacagaat acgaagggcc taagacaaaa ttccacgcgt taatgcagga acagattcat 60  
 aacgaattca cagcggcaca acaatatgtc gcgatcgcg tttatttcga cagcgaagac 120  
 ctgccgcagt tggcgaagca tttttacagc caagcggtcg aggaacgaaa.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 89  
 LENGTH: 822  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 89  
 atgacatggg ccgacgaggt gtcgcgccga catccctttg tggttgctca ccgtgggtgcg 60  
 tcggcggtct ggccggagca tacccttgcc gcctacgacc tggcgctcaa agagggcgcc 120  
 gacggcgtgg aatgtgatgt gcggttgacc cgggacgggc atctggtctg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 90  
 LENGTH: 744  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 90  
 gtgtccgacg gcgaacaagc caaatcacgt cgacgccggg ggcggcgccg cgggcggcgc 60  
 gctgcggcta cagccgagaa tcacatggac gcccaaccgg ccggcgacgc caccgagacc 120  
 ccggcaacgg cgaagcggtc ccggtccgc tcacctgctc gcgggtcgac.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 91  
 LENGTH: 88  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 91  
 Met Lys Ala Lys Val Gly Asp Trp Leu Val Ile Lys Gly Ala Thr Ile  
 1 5 10.

CLM What is claimed is:  
 1. A method for inducing an immune response to latent **tuberculosis** in an individual, said method comprising the step of delivering a composition comprising one or more polypeptides or fragments thereof,  
 2. The method according to claim 1, wherein said individual is infected by a virulent mycobacterium, e.g. M. **tuberculosis**, and is not vaccinated with BCG against **tuberculosis**.

6. A therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection, . . . vaccine according to claim 9 where the fusion partners is selected from the group consisting of ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

13. A multiphase vaccine according to claim 12 where the antigen components with prophylactic activity comprises ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein or MPT32.

18. A method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 6.

19. A method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the vaccine according to claim 12.

20. A method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being, comprising application or intradermally injecting, in the animal, . . . encoding these polypeptides, a positive skin response at the location of injection or application being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection or application being indicative of the animal not having **tuberculosis**.

22. A method of diagnosing Mycobacterium **tuberculosis** infection in a subject comprising: (a) contacting a polypeptides or fragments hereof, which polypeptides are expressed during the latent stage. . . detecting binding of an antibody to said polypeptide, said binding being an indication that said subject is infected by Mycobacterium **tuberculosis** or is susceptible to Mycobacterium **tuberculosis** infection.

L3 ANSWER 14 OF 14 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M.  
**tuberculosis**  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

TI Nucleic acid fragments and polypeptide fragments derived from *M. tuberculosis*

IN Andersen, Peter, Bronshoj, DENMARK

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, . . . )

SUMM [0001] The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the *Mycobacterium tuberculosis*, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from *M. tuberculosis* which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with *M. tuberculosis*. The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.

SUMM [0002] Human *tuberculosis* (hereinafter designated "TB") caused by *Mycobacterium tuberculosis* is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of *M. tuberculosis*.

SUMM [0005] Immunity to *M. tuberculosis* is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations; . . .

SUMM [0006] Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from *M. tuberculosis* during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested. . .

SUMM . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from *M. tuberculosis*. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . the Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21 respectively), shows homology to two *M. tuberculosis* DNA sequences, orf19A and orf23. The two sequences, orf19a and orf23, encode to putative proteins CFP19A and CFP23 with the. . .

SUMM [0011] The present invention is also based on the identification of a number of putative antigens from *M. tuberculosis* which are not present in *Mycobacterium bovis* BCG strains. The nucleotide sequences encoding these putative antigens are: *rd1*-orf2, *rd1*-orf3, *rd1*-orf4, *rd1*-orf5, *rd1*-orf5, *rd1*-orf9a, and *rd1*-orf9b.

SUMM	58		
CFP28	22		
CFP29	23	15	16
CFP30A	85	59	60
CFP30B	171	144	145
CFP50	86	61	62
MPT51		41	42
CWP32	77	152	153
RD1-ORF8		67	68
RD1-ORF2		71	72

RD1-ORF9B	69	70
RD1-ORF3	87	88
RD1-ORF9A	93	94
RD1-ORF4	89	90
RD2-ORF5	91	92
MPT59-		172
ESAT6		
ESAT6-		173
MPT59		
SUMM		

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell.

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the M. **tuberculosis** derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48, . . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by Mycobacterium bovis BCG and also at least. . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of M. **tuberculosis**, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance.

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g.. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals.

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which.

SUMM [0033] The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are Mycobacterium **tuberculosis**, Mycobacterium bovis, Mycobacterium bovis BCG, and Mycobacterium africanum.

SUMM . . . other short peptide sequences), whereas the product which can

be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and.

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenged infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml, . . .

SUMM [0050] 3) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a S-cell epitope derived from the M. **tuberculosis** protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first. . .

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the M. **tuberculosis** proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin. . .

SUMM [0078] isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. M. smegmatis, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extracellular antigens, or because of their absence in M. bovis BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the M. **tuberculosis** complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act.

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as. . .

SUMM [0116] The invention also relates to a method of diagnosing TB caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising

intradermally injecting, in the animal, a polypeptide. . . .

SUMM . . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described. . . .

SUMM . . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that M. **tuberculosis**, e.g. esat-6 is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as M. . . . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have. . . .

SUMM . . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . . .

DRWD [0128] FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with M. **tuberculosis**. Mice were given a challenge of M. **tuberculosis** and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of. . . .

DRWD . . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with M. **tuberculosis** and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN- $\gamma$  was investigated

DRWD . . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in M. **tuberculosis** H37Rv.

DETD [0135] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10.sup.4 M. **tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were. . . .

DETD . . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive. . . .

DETD [0140] The recombinant  $\lambda$ gt11 M. **tuberculosis** DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB. . . .

DETD . . . . In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . . .

DETD [0150] Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+(Stratagene) and used to transform E. coli. . . .

DETD . . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the M. **tuberculosis** genome was performed in the Sanger database (Sanger Mycobacterium **tuberculosis** database):

DETD . . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and M. **tuberculosis** and M. bovis has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . . (Harboe et al., 1996), later 3 large deletions in BCG have been identified (Mahairas et al., 1996). The region named RD1 includes the gene encoding ESAT-6 and an other (RD2) the gene encoding MPT64. Both antigens have been shown to have. . . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new M. **tuberculosis** specific diagnostic antigens as well as antigens for a new vaccine against TB,

the **RD1** region (17.499 bp) of *M. tuberculosis* H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted. . . have possible diagnostic and/or vaccine potential, as they are deleted from all known BCG strains. The predicted ORFs include ESAT-6 (**RD1**-ORF7) and CFP10 (**RD1**-ORF6) described previously (Srensen et al., 1995), as a positive control for the ability of the algorithm. In the present is.

DETD [0176] Seven open reading frames (ORF) from the 17,499 kb **RD1** region (Accession no. U34848) with possible diagnostic and vaccine potential have been identified and cloned.

DETD [0177] Identification of the ORF's **rdl**-orf2, **rdl**-orf3, **rdl**-orf4, **rdl**-orf5, **rdl**-orf2, **rdl**-orf9a, and **rdl**-orf9b.

DETD [0178] The nucleotide sequence of **rdl**-orf2 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of **RD1**-ORF2 is set forth in. . .

DETD [0179] The nucleotide sequence of **rdl**-orf3 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 88.

DETD [0180] The nucleotide sequence of **rdl**-orf4 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 90.

DETD [0181] The nucleotide sequence of **rdl**-orf5 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 92.

DETD [0182] The nucleotide sequence of **rdl**-orf8 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 68.

DETD [0183] The nucleotide sequence of **rdl**-orf9a from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 94.

DETD [0184] The nucleotide sequence of **rdl**-orf9b from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of **RD1**-ORF2 is set forth in SEQ ID NO: 70.

DETD [0185] The DNA sequence **rdl**-orf2 (SEQ ID NO: 71) contained an open reading frame starting with an ATG codon at position 889-891 and ending with a termination codon (TAA) at position 2662-2664 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 72) contains 591 residues corresponding to a molecular weight of 64,525.

DETD [0186] The DNA sequence **rdl**-orf3 (SEQ ID NO: 87) contained an open reading frame starting with an ATG codon at position 2807-2809 and ending with a termination codon (TAA) at position 3101-3103 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 88) contains 98 residues corresponding to a molecular weight of 9,799.

DETD [0187] The DNA sequence **rdl**-orf4 (SEQ ID NO: 89) contained an open reading frame starting with a GTG codon at position 4014-4012 and ending with a termination codon (TAG) at position 3597-3595 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 90) contains 139 residues corresponding to a molecular weight of 14,210.

DETD [0188] The DNA sequence **rdl**-orf5 (SEQ ID NO: 91) contained an open reading frame starting with a GTG codon at position 3128-3130 and ending with a termination codon (TGA) at position 4241-4243 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 92) contains 371 residues corresponding to a molecular weight of 37,647.

DETD [0189] The DNA sequence **rdl**-orf8 (SEQ ID NO: 67) contained an open reading frame starting with a GTG codon at position 5502-5500 and ending with a termination codon (TAG) at position 5084-5082 (position numbers referring to the location in **RD1**), and the deduced amino acid sequence (SEQ ID NO: 68) contains 139 residues with a molecular weight of 11,737.

DETD [0190] The DNA sequence **rdl**-orf9a (SEQ ID NO: 93) contained an open reading frame starting with a GTG codon at position 6146-6148 and ending with a termination codon (TAA) at position 7070-7072 (position

numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 94) contains 308 residues corresponding to a molecular weight of 33,453.

DETD [0191] The DNA sequence **rd1-orf9b** (SEQ ID NO: 69) contained an open reading frame starting with an ATG codon at position 5072-5074 and ending with a termination codon (TAA) at position 7070-7072 (position numbers referring to the location in **RD1**). The deduced amino acid sequence (SEQ ID NO: 70) contains 666 residues corresponding to a molecular weight of 70,650.

DETD [0192] Cloning of the ORF's **rd1-orf2**, **rd1-orf3**, **rd1-orf4**, **rd1-orf5**, **rd1-orf8**, **rd1-orf9a**, and **rd1-orf9b**.

DETD [0193] The ORF's **rd1-orf2**, **rd1-orf3**, **rd1-orf4**, **rd1-orf5**, **rd1-orf8**, **rd1-orf9a** and **rd1-orf9b** were PCR cloned in the pMST24 (Theisen et al., 1995) (**rd1-orf3**) or the pQE32 (QIAGEN) (**rd1-orf2**, **rd1-orf4**, **rd1-orf5**, **rd1-orf8**, **rd1-orf9a** and **rd1-orf9b**) expression vector. Preparation of oligonucleotides and PCR amplification of the **rd1-orf** encoding genes, was carried out as described in example 2. Chromosomal DNA from **M. tuberculosis** H37Rv was used as template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from the **RD1** region (Accession no. U34848). The oligonucleotide primers were engineered to include an restriction enzyme site at the 5' end and.

DETD [0194] **rd1-orf2**.

DETD [0195] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf2**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf2** was subcloned in pQE32, giving pT096.

DETD [0196] **rd1-orf3**.

DETD [0197] A SmaI site was engineered immediately 5' of the first codon of **rd1-orf3**, and a NcoI site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf3** was subcloned in pMST24, giving pT087.

DETD [0198] **rd1-orf34**.

DETD [0199] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf4**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf4** was subcloned in pQE32, giving pT089.

DETD [0200] **rd1-orf5**.

DETD [0201] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf5**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf5** was subcloned in pQE32, giving pT088.

DETD [0202] **rd1-orf8**.

DETD [0203] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf8**, and a NcoI site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf8** was subcloned in pMST24, giving pT098.

DETD [0204] **rd1-orf9a**.

DETD [0205] A BamHI site was engineered immediately 5' of the first codon of **rd1-orf9a**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf9a** was subcloned in pQE32, giving pT091.

DETD [0206] **rd1-orf9b**.

DETD [0207] A ScaI site was engineered immediately 5' of the first codon of **rd1-orf9b**, and a Hind III site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf9b** was subcloned in pQE32, giving pT090.

DETD [0209] Purification of recombinant **RD1-ORF2**, **RD1-ORF3**, **RD1-ORF4**, **RD1-ORF5**, **RD1-ORF8**, **RD1-ORF9a** and **RD1-ORF9b**.

DETD . . . the His-r**RD1-ORF**'s were pooled and subsequently dialysed extensively against 25 mM Hepes, pH 8.0 before use.

Sequence of the **rd1**-orf's oligonucleotides.sup.a.  
 Orientation and  
 oligonucleotide Sequences (5' → 3')  
 Position (nt)

Sense

PD1-ORF2f	CTGGGGATCCGCATGACTGCTGAACCG	886-903
PD1-ORF3f	CTTCCCGGGATGGAAAAAATGTAC	
	2807-2822	
<b>RD1</b> -ORF4f	GTAGGATCCTAGGAGACATCAGCGGC	
	4028-4015	
<b>RD1</b> -ORF5f	CTGGGGATCCGCGTGATCACCATGCTGTGG	
	3028-3045	
<b>RD1</b> -ORF8f	CTCGGATCCTGTGGGTGCAGGTCCGGCGATGGGC	
	5502-5479	
<b>RD1</b> -ORF9af	GTGATGTGAGCTCAGGTGAAGAAGGTGAAG	
	6144-6160	
<b>RD1</b> -ORFF9bf	GTGATGTGAGCTCCTATGGCGGCCGACTACGAC	
	5072-5089	

Antisense

PD1-ORF2r	TGCAAGCTTTTAACCGGCGCTTGGGGGTGC
	2664-2644
<b>RD1</b> -ORF3r	GATGCCATGGTTAGGCGAAGACGCCCGGC
	3103-3086
<b>RD1</b> -ORF4r	CGATCTAAGCTTGGCAATGGAGGTCTA
	3582-3597
<b>RD1</b> -ORF5r	TGCAAGCTTTCACCAGTCGTCCTCTTCGTC
	4243-4223
<b>RD1</b> -ORF8r	CTCCCATGGCTACGACAAGCTCTTCCGGCCCGC
	5083-5105
PD1-ORF9a/br	CGATCTAAGCTTTCACGACGTCCAGCC
	7073-7056

.sup.aThe oligonucleotides were constructed from the Accession number U34484 nucleotide sequence (Mahairas et al., 1996). Nucleotides (nt). . .

DETD [0211] The nucleotide sequences of **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a, and **rd1**-orf9b from **M. tuberculosis** H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of **rd1**-orf2, **rd1**-orf3, **rd1**-orf4 **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a, and **rd1**-orf9b are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 94, and 70, respectively.

DETD . . . the Linocin M18 protein from *Brevibacterium linens*, a set of degenerated primers were constructed for PCR cloning of the **M. tuberculosis** gene encoding CFP29. PCR reactions were containing 10 ng of **M. tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 µM of each of the four nucleotides (Boehringer).

DETD . . . first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0230] ([http://www.sanger.ac.uk/projects/M-tuberculosis/blast\\_server](http://www.sanger.ac.uk/projects/M-tuberculosis/blast_server)).

DETD [0231] This program identified a *Mycobacterium tuberculosis* sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29.

DETD . . . sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD . . . protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in **M. tuberculosis** culture filtrate is 175 amino acids. This gives a theoretical molecular weigh at 18517 Da and a pI at 6.8.. . .

DETD . . . with gene specific primers, for recombinant expression in *E. coli* of the proteins. PCR reactions contained 10 ng of **M. tuberculosis** chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides

(Boehringer. . . . .

DETD . . . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium tuberculosis database:

DETD [0296] <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD . . . . . were found in the Sanger database. This could be due to the fact that only approximately 70% of the M. tuberculosis genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining. . . . .

DETD . . . . . CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two Mycobacterium tuberculosis sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second, . . . . .

DETD [0336] CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative M. tuberculosis thymidylate synthase 450 aa accession No p28176).

DETD [0343] PCR reactions contained 10 ng of M. tuberculosis chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . . . .

DETD . . . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium tuberculosis genome database:

DETD [0366] <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD [0374] PCR reactions contained 10 ng of M. tuberculosis chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . . . .

DETD . . . . . were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from M. tuberculosis H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994).. . . .

DETD [0392] The nucleotide sequence of the cloned 952 bp M. tuberculosis H37Rv PCR fragment, pT052, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . . . .

DETD . . . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. tuberculosis H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . . . .

DETD . . . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. tuberculosis. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . . . .

DETD [0415] PCR reactions contained 10 ng of M. tuberculosis chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . . . .

DETD . . . . . same high level as ST-CF.

TABLE 5

IFN- $\gamma$  release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. tuberculosis after stimulation with native antigens.

Antigen.sup.a	IFN- $\gamma$ (pg/ml).sup.b
ST-CF	12564
CFP7	ND.sup.d
CFP9	ND
CFP17	9251
CFP20	2388
CFP21	10732.

DETD [0432] The skin test activity of the purified proteins was tested in M. tuberculosis infected guinea pigs.

DETD [0433] 1 group of guinea pigs was infected via an ear vein with

1+10<sup>.sup.4</sup> CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS.

After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was.

DETD . . . significant Delayed Type Hypersensitivity (DTH) reaction.

TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10<sup>.sup.4</sup> CFU of M. **tuberculosis**, after stimulation with native antigens.

Antigen <sup>.sup.a</sup>	Skin reaction (mm) <sup>.sup.b</sup>
---------------------------	--------------------------------------

Control	2.00
PPD <sup>.sup.c</sup>	15.40 (0.53)
CFP7	ND <sup>.sup.e</sup>
CFP9	ND
CFP17	11.25. . .

DETD . . . animal models.

TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10<sup>.sup.4</sup> CFU of M. **Tuberculosis**.

Antigen <sup>.sup.a</sup>	Skin reaction (mm) <sup>.sup.b</sup>
---------------------------	--------------------------------------

Control	2.9 (0.3)
PPD <sup>.sup.a</sup>	14.5 (1.0)
CFP 7a	13.6 (1.4)
CFP 17	6.8 (1.9)
CFP 20.	

DETD . . . and A.SW(H-2<sup>.sup.s</sup>) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10<sup>.sup.4</sup> M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were.

DETD . . . female C57BL/6j(H-2<sup>.sup.b</sup>) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10<sup>.sup.4</sup> M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

	++	+++	+	
rCFP29	+++	+++	+++	++
rMPT51	+	-	-	-

Mouse IFN-γ release during recall of memory immunity to M.

**tuberculosis**.

-: no response;

+: 1/3 of ST-CF;

++: 2/3 of ST-CF;

+++: level of ST-CF.

DETD . . . +++

rCFP21	+++
rCFP22	-
rCFP29	+
rCFP25	+++
rMPT51	+

Mouse IFN-γ release 14 days after primary infection with M.

**tuberculosis**.

-: no response;

+: 1/3 of ST-CF;

++: 2/3 of ST-CF;

+++: level of ST-CF.

DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD [0472] 6 weeks after the last immunization the mice were aerosol challenged with 5+10<sup>.sup.6</sup> viable Mycobacterium **tuberculosis** /ml. After 6 weeks of infection the mice were

killed and the number of viable bacteria in lung and spleen. . .

DETD [0476] Species distribution of cfp7, cfp9, mpt51, **rdl**-orf2, **rdl**-orf3, **rdl**-orf4, **rdl**-orf5, **rdl**-orf8, **rdl**-orf9a and **rdl**-orf9b as well as of cfp7a, cfp7b, cfp10a, cfp17, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a.

DETD [0477] Presence of cfp7, cfp9, mpt51, **rdl**-orf2, **rdl**-orf3, **rdl**-orf4, **rdl**-orf5, **rdl**-orf8, **rdl**-orf9a and **rdl**-orf9b in different mycobacterial species.

DETD [0478] In order to determine the distribution of the cfp7, cfp9, mpt51, **rdl**-orf2, **rdl**-orf3, **rdl**-orf4, **rdl**-orf5, **rdl**-orf8, **rdl**-orf9a and **rdl**-orf9b genes in species belonging to the *M. tuberculosis*-complex and in other mycobacteria PCR and/or Southern blotting was used. The bacterial strains used are listed in TABLE 10. Genomic. . .

DETD . . . were used in order to determine the distribution of the cfp7, cfp9 and mpt51 gene in species belonging to the **tuberculosis**-complex and in other mycobacteria. The bacterial strains used are listed in TABLE 10. PCR was performed on genomic DNA prepared. . .

DETD . . . bp). cfp9: stR3 and stF1 (351 bp).

TABLE 10

#### Mycobacterial strains used in this Example.

Species and strain(s)	Source
1. <i>M. tuberculosis</i>	H 3 7 R vATCC.sup.a (ATCC 27294)
2.	H 3 7 R aATCC (ATCC 25177)
3.	Erdman      Obtained from A.
DETD . . . plc, Little Chalfont, United Kingdom) with a vacuum transfer device (Milliblot, TM-v; Millipore Corp., Bedford, Mass.). The cfp7, cfp9, mpt51, <b>rdl</b> -orf2, <b>rdl</b> -orf3, <b>rdl</b> -orf4, <b>rdl</b> -orf5, <b>rdl</b> -orf8, <b>rdl</b> -orf9a and <b>rdl</b> -orf9b gene fragments were amplified by PCR from the plasmids pRVN01, pRVN02, pT052, pT087, pT088, pT089, pT090, pT091, pT096 or pT098.	
DETD [0487] cfp7, cfp9 and mpt51 were found in the <i>M. tuberculosis</i> coinplex including BCG and the environmental mycobacteria; <i>M. avium</i> , <i>M. kansasii</i> , <i>M. marinum</i> , <i>M. intracellulare</i> and <i>M. flavescens</i> . cfp9 was. . .	
DETD [0489] There is a strong band at around 26 kDa in <i>M. tuberculosis</i> H37Rv, Ra, Erdman, <i>M. bovis</i> AN5, <i>M. bovis</i> BCG substrain Danish 1331 and <i>M. africanum</i> . No band was seen in the region in any other tested mycobacterial strains.	

TABLE 13a

Interspecies analysis of the **rdl**-orf2, **rdl**-orf3, **rdl**-orf4, **rdl**-orf5, **rdl**-orf8, **rdl**-orf9a and **rdl**-orf9b genes by Southern blotting.

Species and strain	<b>rdl</b> -orf2	<b>rdl</b> -orf3	<b>rdl</b> -orf4	<b>rdl</b> -orf5	<b>rdl</b> -orf8	<b>rdl</b> -orf9a	<b>rdl</b> -orf9b
1. <i>M. tub.</i> H37Rv	+	+	+	+	+	+	+
2. <i>M. bovis</i>	+	+	+	+	+	N.D.	+
3. <i>M.</i> . . .							
DETD [0490] Positive results for <b>rdl</b> -orf2, <b>rdl</b> -orf3, <b>rdl</b> -orf4, <b>rdl</b> -orf5, <b>rdl</b> -orf8; <b>rdl</b> -orf9a and <b>rdl</b> -orf9b were only obtained when using genomic DNA							

from M. **tuberculosis** and M. bovis, and not from M. bovis BCG or other mycobacteria analyzed except **rd1**-orf4 which also was found in M. marinum.

DETD [0492] Southern blotting was carried out as described for **rd1**-orf2, **rd1**-orf3, **rd1**-orf4, **rd1**-orf5, **rd1**-orf8, **rd1**-orf9a and **rd1**-orf9b. The **cfp7a**, **cfp7b**, **cfp10a**, **cfp17**, **cfp20**, **cfp21**, **cfp22**, **cfp22a**, **cfp23**, **cfp25** and **cfp25a** gene fragments were amplified by PCR from. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 381

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

```
ggccgcccgt acctatgtgg ccgccgatgc tgcggacgcg tcgacctata ccgggttctg      60
atcgaaccct gctgaccgag aggacttgtg atgtcgcaaa tcatgtacaa ctaccccgcg      120
atgttgggtc acgccgggga tatggccgga tatgccggca cgctgcagag. . .
```

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 96

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 2

Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly

1 . . . . . 5 . . . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 3

LENGTH: 467

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 3

```
gggtagcccg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg      60
gcgacggcgt cataaaccgg gacggcacct tggtggcggg cccgcggtg ctgacgcccg      120
acgagtacaa ctcccggctg gtggccgccg acccggagtc caccgcggcg. . .
```

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 4

LENGTH: 108

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 4

Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly

1 . . . . . 5 . . . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 5

LENGTH: 889

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 5

```
cgggctctgca cggatccggg ccgggcaggg caatcgagcc tgggatccgc tggggtgcgc      60
acatcgcgga cccgtgcgcg gtacggtcga gacagcggca cgagaaagta gtaagggcga      120
taataggcgg taaagagtag cggaagccg gccgaacgac tcggtcagac. . .
```

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 6

LENGTH: 162

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 6

Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu

1 . . . . . 5 . . . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 7

LENGTH: 898

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 7

```
tcgactccgg cgccaccggg caggatcacg gtgtcgacgg ggtcgccggg gaatcccacg      60
ataaccactc ttcgcgcat gaatgccagt gttggccagg cgctggcctg gcgtccacgc      120
cacacaccgc acagattagg acacgccggc ggcgcagccc tgcccgaag. . .
```

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 8

LENGTH: 165

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 8

Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu

1

5.

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 9

LENGTH: 1054

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 9

ataatcagct caccgttggg accgacctcg accaggggtc ctttgtgact gccgggcttg 60

acgcggacga ccacagagtc ggtcatcgcc taaggctacc gttctgacct ggggctgcgt 120

gggcgccgac gacgtgaggc acgtcatgtc tcagcggccc accgccacct. . .

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 10

LENGTH: 217

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 10

Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr

1

5.

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 11

LENGTH: 949

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 11

agccgctcgc gtgggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60

gtccgggccc aggcctgcgc tcaataactc ggtcaagttc cttcacagac tgccatcact 120

ggcccgctcg cgggctcggtt gcgggtgcgc cgcgtgcggg tttgtgttcc. . .

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 12

LENGTH: 182

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 12

Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr

1

5.

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 13

LENGTH: 1060

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 13

tggaccttca ccggcggtcc cttcgcttcg ggggcgacac ctaacatact ggtcgtcaac 60

ctaccgcgac accgctggga ctttgtgccca ttgccggcca ctccggggccg ctgcggcctg 120

gaaaaaattgg tcgggcacgg gcggccgcgg gtcgctacca tcccactgtg. . .

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 14

LENGTH: 219

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 14

Met Gly Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro

1

5.

## DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 15

LENGTH: 1198

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 15

cagatgctgc gcaacatggt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60

ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120

ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgct. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 16

LENGTH: 265

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 16

Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp

1

5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 17

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: VARIANT

LOCATION: (1)

OTHER INFORMATION: Ala is Ala or Ser

SEQUENCE: 17

Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 18

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 18

Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu

1

5

10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 19

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (3)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 19

Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 20

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 20

Thr Asn Ser Pro Leu Ala Thr Ala Thr Leu His Thr Asn

1

5

10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 21

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (2)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 21

Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 22

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (1)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 22

Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 23

LENGTH: 19

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 23

Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp

1

5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 24

LENGTH: 34

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 24

cccggctcga gaacctstac cgcgacctsg csc

34

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 25

LENGTH: 37

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 25

gggccggatc cgasgcsgcg tccttsacsg gytgcc

37

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 26

LENGTH: 28

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 26

ggaagcccca tatgaacaat ctctaccg

28

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 27

LENGTH: 32

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 27

cgcgctcagc ccttagtgac tgagcgcgac cg

32

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 28

LENGTH: 24

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 28

ctcgaattcg ccgggtgcac acag

24

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 29

LENGTH: 25

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 29

ctcgaattcg ccccatatcg agaac

25

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 30

LENGTH: 15

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 30

gtgtatctgc tggac

15

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 31

LENGTH: 15

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 31

ccgactggct ggccg

15

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 32

LENGTH: 24

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 32	
gaggaattcg cttagcggat cgca	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 33	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 33	
cccacattcc gttgg	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 34	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 34	
gtccagcaga tacac	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 35	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 35	
gtacgagaat tcatgtcgca aatcatg	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 36	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 36	
gtacgagaat tcgagcttgg ggtgccg	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 37	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 37	
cgattccaag cttgtggccg ccgaccg	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 38	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 38	
cgttagggat cctcatcgcc atggtggttg	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 39	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 39	
cgttagggat ccggttccac tgtgcc	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 40	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 40	
cgttagggat cctcaggtct ttctgatg	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 41	
LENGTH: 952	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 41	
gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg	60
cgctgctgcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggg gtcgcggtag	120
ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg. . .	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 42

LENGTH: 299

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 42

Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu

1

5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 43

LENGTH: 27

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 43

gcaacacccg ggatgtcgca aatcatg

27

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 44

LENGTH: 27

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 44

gtaacacccg gggtagccgc cgacccg

27

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 45

LENGTH: 37

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 45

ctactaagct tggatcccta gccgccccat ttggcgg

37

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 46

LENGTH: 38

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 46

ctactaagct tccatgggtca ggtcttttcg atgcttac

38

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 47

LENGTH: 450

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 47

gtgccgcgct ccccagggtt cttatgggtc gatatacctg agtttgatgg aagtccgatg

60

accagcagtc agcatacggc atggccgaaa agagtggggt gatgatggcc gaggatgttc

120

gcgccgagat cgtggccagc gttctcgaag tcgttgtaa cgaaggcgat.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 48

LENGTH: 71

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 48

Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val

1

5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 49

LENGTH: 750

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 49

gggtacccat cgatggggttg cggttcggca ccgaggtgct aacgcacttg ctgacacact

60

gctagtcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac

120

ttcaccggac ccgtatgccg cgctgccccaa gctgccgtcc ttcagcctga.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 50

LENGTH: 176

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 50

Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser

1

5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 51

LENGTH: 800

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 51

tcatgaggtt catcggggtg atccccacgcc cgcagccgca ttcggggccgc tggcgagccg 60

gtgccgcacg ccgctcacc agcctgggtg ccgcccctt tgcggcgccg acactgttgc 120

ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 52

LENGTH: 226

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 52

Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala

1

5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 53

LENGTH: 700

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 53

ctaggaaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt 60

aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag 120

gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 54

LENGTH: 181

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 54

Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln

1

5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 55

LENGTH: 950

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 55

tgggctcggc actggctctc ccacggtggc gcgctgattt ctccccacgg taggcgttgc 60

gacgcatggt cttcaccgtc tatccacagc taccgacatt tgctccggct ggatcgcggg 120

taaaattccg tcgtgaacaa tcgacccatc cgctgctga catccggcag.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 56

LENGTH: 262

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 56

Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu

1

5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 57

LENGTH: 1000

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 57

cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60

cttcgtccgc gcatacgtcc aaaaggggcg acagtgcctt ggccgttgcc cgatcgccctg 120

tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 58

LENGTH: 291

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 58

Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 59

LENGTH: 900

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 59

ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 60

gagaagtga gatttccgtat ttcattctcg ctgagcaggc gatgcgcgag cgcagcgagt 120

tggcgcgtaa gggcattgcg cgggcaaaaa gcgtggtggc gctggcctat. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 60

LENGTH: 248

TYPE: PRT

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 60

Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 61

LENGTH: 1560

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 61

gagtcattgc ctggctcgcg tcattccgta ctatgcggtt gtcggacttg acctactggg 60

tcaggccgac gagcactcga ccattagggt aggggccgtg acccactatg acgtcgtcgt 120

tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 62

LENGTH: 464

TYPE: PRT

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 62

Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 63

LENGTH: 550

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 63

ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60

gtagtcaccc agtaccacac accaggaagg accgcccac atggcaaagc tctccaccga 120

cgaactgctg gacgcgttca aggaaatgac cctgttggag ctctccgact. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 64

LENGTH: 130

TYPE: PRT

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 64

Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 65

LENGTH: 900

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 65

tgaacgccat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60

tcttccccag gtcgtacagt cgggccatgg ccattgaggt ttcggtgttg cgggttttca 120

ccgattcaga cgggaatttc ggtaatccgc tgggggtgat caacgccagc. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 66

LENGTH: 228

TYPE: PRT

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 66

Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 67

LENGTH: 500

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 67

gtttgtggtg tcggtggtct ggggggcgcc aactgggatt cggttggggt ggggtgcaggt 60

ccggcgatgg gcatcgagg tgtgggtggt ttgggtgggg ccggttcggg tccggcgatg 120

ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 68

LENGTH: 139

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 68

Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 69

LENGTH: 2050

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 69

agcgactct gagaggttgt catggcgggc gactacgaca agctcttccg gccgcacgaa 60

ggtatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120

ccgccggcgc ccgcatcggc aaacctaccg aagccaacg gccagactcc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 70

LENGTH: 666

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 70

Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 71

LENGTH: 1890

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 71

gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgcagcga 60

tgaggaggag cggcgcgcat gactgctgaa ccggaagtac ggacgctgcg cgagggtgtg 120

ctggaccagc tcggcactgc tgaatcgct gcgtacaaga tgtggctgcc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 72

LENGTH: 591

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 72

Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 73

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 73

Asp Pro Val Asp Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly

1 5 10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 74

LENGTH: 14

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

FEATURE:

NAME/KEY: UNSURE

LOCATION: (14)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 74  
 Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 75  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (5)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 75  
 Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 76  
 LENGTH: 14  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: VARIANT  
 LOCATION: (3)  
 OTHER INFORMATION: Ala is Ala or Gln  
 SEQUENCE: 76  
 Val Ile Ala Gly Met Val Thr His Ile His Xaa. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 77  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 77  
 Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 78  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 78  
 Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 79  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 79  
 Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 80  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: VARIANT  
 LOCATION: (4)  
 OTHER INFORMATION: Asp is Asp or Glu  
 SEQUENCE: 80  
 Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 81  
 LENGTH: 50  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 81  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val

1 5.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 82  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 82  
Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser

1 5 10.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 83  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 83  
Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln

1 5 10.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 84  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 84  
Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala

1 5 10.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 85  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
FEATURE:  
NAME/KEY: UNSURE  
LOCATION: (10)  
OTHER INFORMATION: Xaa is unknown  
SEQUENCE: 85  
Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg.

DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 86  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 86  
Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr

1 5 10.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 87  
LENGTH: 450  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 87  
agcccggttaa tcgagttcgg gcaatgctga ccatacgggtt tgtttccggc tataaccgaa 60  
cggtttgtgt acgggataca aatacaggga gggaagaagt aggcaaatgg aaaaaatgtc 120  
acatgatccg atcgtgccg acattggcac gcaagtgagc gacaacgctc.

DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 88  
LENGTH: 98  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 88  
Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln

1 5.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 89  
LENGTH: 460  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 89  
gcaaccggct tttcgatcag ctgagacatc agcggcgctgc gggtaacga cccacctgcg 60

ccaggtagcg actccgcgcg cagcaggccc gcgcccgcgc tggggcctga tccaccagcc 120  
agcggatggt tcgacagcgg actggtgccg agcaggccca tctgcgcggc. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 90  
LENGTH: 139  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 90  
Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser  
1 5. . . . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 91  
LENGTH: 1200  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 91  
taataggccc ccaacacatc ggaggggagtg atcaccatgc tgtggcacgc aatgccaccg 60  
gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120  
gcgggatggc agacgctttc ggcggctctg gacgctcagg ccgctcgagtt. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 92  
LENGTH: 371  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 92  
Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala  
1 5. . . . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 93  
LENGTH: 1000  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 93  
gacgcgacac agaaatcctt aaggccggcg gccaaaggggc cgaaggtgaa gaaggtgaag 60  
ccccagaaac cgaaggccac gaagccgccc aaagtgggtg cgcagcgcgg ctggcgacat 120  
tgggtgcatg cgttgacgcg aatcaacctg ggcctgtcac ccgacgagaa. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 94  
LENGTH: 308  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 94  
Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys  
1 5. . . . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 95  
LENGTH: 34  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 95  
aagagtagat ctatgatggc cgaggatggt cgcg 34  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 96  
LENGTH: 27  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 96  
cggcgacgac ggatcctacc gcgtcgg 27  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 97  
LENGTH: 28  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 97  
ccttgggaga tctttggacc ccggttgc 28  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 98  
LENGTH: 25

TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 98	
gacgagatct tatgggctta ctgac	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 99	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 99	
ccccccagat ctgcaccacc ggcacgcggcg ggc	33
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 100	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 100	
gcggcggatc cgttgcttag ccgg	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 101	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 101	
ccggctgaga tctatgacag aatacgaagg gc	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 102	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 102	
ccccgccagg gaactagagg cggc	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 103	
LENGTH: 38	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 103	
ctgccgagat ctaccacat tgtcgcgctg aaataccc	38
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 104	
LENGTH: 25	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 104	
cgccatggcc ttacgcgcca actcg	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 105	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 105	
ggcggagatc tgtgagtttt ccgtatttca tc	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 106	
LENGTH: 25	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 106	
cgcgtcgagc catgggttagg cgcag	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 107	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 107	
gaggaagatc tatgacaact tcacccgacc cg	32
DETD SEQUENCE CHARACTERISTICS:	

SEQ ID NO: 108	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 108	
catgaagcca tggcccgag gctgcatg	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 109	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 109	
ggccgagatc tgtgaccac tatgacgtcg tcg	33
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 110	
LENGTH: 36	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 110	
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc	36
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 111	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 111	
ccgggagatc tatggcaaag ctctccaccg acg	33
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 112	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 112	
cgctgggcag agctacttga cggtgacggt gg	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 113	
LENGTH: 36	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 113	
ggcccagatc tatggccatt gaggtttcgg tgttgc	36
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 114	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 114	
cgccgtgttg catggcagcg ctgagc	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 115	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 115	
ggacgttcaa gcgacacatc gccg	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 116	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 116	
cagcacgaac gcgccgtcga tggc	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 117	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 117	

acagatctgt gacggacatg aacccg	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 118	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 118	
ttttccatgg tcacggggccc ccggtact	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 119	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 119	
acagatctgt gcccattggca cagata	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 120	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 120	
tttaagcttc taggcgccc gcgcggc	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 121	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 121	
acagatctgc gcatgcggat ccgtgt	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 122	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 122	
ttttccatgg tcatccggcg tgatcgag	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 123	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 123	
acagatctgt aatggcagac tgtgat	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 124	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 124	
ttttccatgg tcaggagatg gtgatcga	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 125	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 125	
acagatctgc cggctacccc ggtgcc	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 126	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 126	
ttttccatgg ctattgcagc tttccggc	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 127	
LENGTH: 50	
TYPE: PRT	

ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 127  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 128  
 LENGTH: 49  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 128  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 129  
 LENGTH: 50  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 129  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 130  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 130  
 ccgggagatc tatggcaaag ctctccaccg acg 33  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 131  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 131  
 cgctgggcag agctacttga cggtgacggt gg 32  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 132  
 LENGTH: 36  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 132  
 ggcgccggca agcttgccat gacagagcag cagtgg 36  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 133  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 133  
 cgaactcgcc ggatcccgtg ttctgc 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 134  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 134  
 ggcaaccgcg agatctttct cccggccggg gc 32  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 135  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 135  
 ggcaagcttg ccggcgcccta acgaact 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 136  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 136

ggaccagat ctatgacaga gcagcagtgg 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 137  
 LENGTH: 47  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 137  
 ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg 47  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 138  
 LENGTH: 44  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 138  
 gttcgcaaag cttttctccc ggccggggct gccggtcgag tacc 44  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 139  
 LENGTH: 20  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 139  
 ccttcggtgg atcccgtcag 20  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 140  
 LENGTH: 450  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 140  
 tggcgctgtc accgaggaac ctgtcaatgt cgtcgagcag tactgaaccg ttccgagaaa 60  
 ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120  
 gaagagtgtc tcggccagcg gcgatacctt ggggtgccgtc atcagcgacc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 141  
 LENGTH: 93  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 141  
 Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 142  
 LENGTH: 480  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 142  
 ggtgttcccg cggccgggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60  
 tccaggttca acaaggagac aggcaacatg gcaacacgtt ttatgacgga tccgcacgcg 120  
 atgcgggaca tggcggggccg ttttgaggtg cacgcccaga cgggtggagga.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 143  
 LENGTH: 98  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 143  
 Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 144  
 LENGTH: 940  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 144  
 gccccagtcc tcgatcgctt catcgcttcc accggccgcc agccgaccgc aggccacgtg 60  
 tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120  
 gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 145  
 LENGTH: 261

TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 145  
 Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 146  
 LENGTH: 280  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 146  
 ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacaggggaac 60  
 tgtgaagtgg ttcaacgcgg agaagggggtt cggctttatc gccccgaag acggttccgc 120  
 ggatgtatgt gtccactaca cggagatcca gggaaacgggc ttccgcaccc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 147  
 LENGTH: 67  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 147  
 Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 148  
 LENGTH: 540  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 148  
 atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60  
 acttcgtgtc ccaaatgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120  
 atcagaccct gacgtgcga ctgctggcgg catccgcggg cattctcagc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 149  
 LENGTH: 129  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 149  
 Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 150  
 LENGTH: 400  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 150  
 atagtttggg gaagggtgtcc ataaatgagg ctgtcgttga ccgcattgag cgccggtgta 60  
 ggcgcgctgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120  
 gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 151  
 LENGTH: 110  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 151  
 Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 152  
 LENGTH: 990  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 152  
 aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga ggttccgcag tcgagcgctg 60  
 cgggcccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120  
 aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 153  
 LENGTH: 266

TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 153  
 Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser  
 1 5. . . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 154  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 154  
 ctgagatcta tgaacctacg gcgcc 25  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 155  
 LENGTH: 35  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 155  
 ctcccatggt accctaggac ccgggcagcc ccggc 35  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 156  
 LENGTH: 29  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 156  
 ctgagatcta tgaggctgtc gttgaccgc 29  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 157  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 157  
 ctccccgggc ttaatagttg ttgcaggagc 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 158  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 158  
 gcttagatct atgattttct gggcaaccag gta 33  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 159  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 159  
 gcttccatgg gcgaggcaca ggcgtgggaa 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 160  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 160  
 ctgagatcta gaatgccaca gggaactgtg 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 161  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 161  
 tctccccgggg gtaactcaga gcgagcggac 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 162  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 162  
 ctgagatcta tgaacgtcac cgtatcc 27

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 163  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 163  
 tctcccgggg ctcacccacc ggccacg 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 164  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 164  
 ctgagatcta tggcaacacg ttttatgacg 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 165  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 165  
 ctccccgggt tagctgctga ggatctgcth 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 166  
 LENGTH: 31  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 166  
 ctgaagatct atgccaaga gaagcgaata c 31  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 167  
 LENGTH: 31  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 167  
 cggcagctgc tagcattctc cgaatctgcc g 31  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 168  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 168  
 Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 169  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (15)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 169  
 Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 170  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: VARIANT  
 LOCATION: (1)  
 OTHER INFORMATION: Thr could also be Ala  
 SEQUENCE: 170  
 Thr Arg Phe Met Thr Asp Pro His Ala Met Arg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 171  
 LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 171

Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp

1

5

10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 172

LENGTH: 404

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 172

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His

1

5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 173

LENGTH: 403

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 173

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His His

1

5

CLM What is claimed is:

in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) comprises an amino acid sequence having a sequence identity with the polypeptide defined in a) or the . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, with the proviso that i) the polypeptide fragment is in essentially pure form when consisting of the amino acid.

weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200.000 spleen cells per ml, . . . suspension; and/or 3) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

fragment as defined in any of claims 1-8, and an other polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6 or at least one T-cell epitope thereof, MPB64 or at least one T-cell epitope thereof, MPT64.

first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from MPT59 and/or including a stretch of amino acids which protects the first amino acid sequence from in.

11-13, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment

according to any of claims 1-55, DnaK, GroEL, urease, glutamine. . . .  
. . . sequence of ESAT-6 or of MPT59 and/or the second amino acid sequence  
is the amino acid sequence of a M. **tuberculosis** polypeptide  
selected from the group consisting of a polypeptide fragment according  
to any of claims 1-8, DnaK, GroEL, urease, glutamine. . . .  
. . . according to any of claims 1-20 in the preparation of a  
pharmaceutical composition for the diagnosis of or vaccination against  
**tuberculosis** caused by Mycobacterium **tuberculosis**,  
Mycobacterium africanum or Mycobacterium bovis.

. . . . been administered, the amount of expressed antigen being effective to  
confer substantially increased resistance to infections with  
mycobacteria of the **tuberculosis** complex in an animal,  
including a human being.

. . . . according to claim 23 or 24 in the preparation of a pharmaceutical  
composition for the diagnosis of or vaccination against  
**tuberculosis** caused by Mycobacterium **tuberculosis**,  
Mycobacterium africanum or Mycobacterium bovis.

35. A vaccine for immunizing an animal, including a human being, against  
**tuberculosis** caused by mycobacteria belonging to the  
**tuberculosis** complex, comprising as the effective component a  
non-pathogenic microorganism, wherein at least one copy of a DNA  
fragment comprising a. . . .

44. A transformed cell according to claim 43, which is a bacterium  
belonging to the **tuberculosis** complex, such as a M.  
**tuberculosis** bovis BCG cell.

. . . . polypeptide from a short-term culture filtrate as defined in claim 1;  
or isolating the polypeptide from whole mycobacteria of the  
**tuberculosis** complex or from lysates or fractions thereof, e.g.  
cell wall containing fractions; or synthesizing the polypeptide by  
solid or liquid. . . .

. . . . of claims 1-20, and solubilizing or dispersing the polypeptide in a  
medium for a vaccine, and optionally adding other M.  
**tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant  
substance, or cultivating a cell according to any of claims 37-45, and  
transferring. . . .

48. A method of diagnosing **tuberculosis** caused by  
Mycobacterium **tuberculosis**, Mycobacterium africanum or  
Mycobacterium bovis in an animal, including a human being, comprising  
intradermally injecting, in the animal, a polypeptide. . . .  
composition according to claim 34, a positive skin response at the  
location of injection being indicative of the animal having  
**tuberculosis**, and a negative skin response at the location of  
injection being indicative of the animal not having **tuberculosis**

49. A method for immunising an animal, including a human being, against  
**tuberculosis** caused by mycobacteria belonging to the  
**tuberculosis** complex, comprising administering to the animal the  
polypeptide according to any of claims 1-20, the immunologic composition  
according to claim. . . .

. . . . A method for diagnosing ongoing or previous sensitization in an  
animal or a human being with bacteria belonging to the  
**tuberculosis** complex, the method comprising providing a blood  
sample from the animal or human being, and contacting the sample from  
the. . . .

52. A composition for diagnosing **tuberculosis** in an animal,  
including a human being, comprising a polypeptide according to any of  
claims 1-20, or a nucleic acid. . . .

```
=> e skjot rikke/au
E1      2      SKJOT R L/AU
E2      9      SKJOT R L V/AU
E3      1 --> SKJOT RIKKE/AU
```

E4	2	SKJOT RIKKE L V/AU
E5	17	SKJOT RIKKE LOUISE VINTHER/AU
E6	1	SKJOT V/AU
E7	11	SKJOTH C A/AU
E8	5	SKJOTH C AMBELAS/AU
E9	4	SKJOTH CARSTEN AMBELAS/AU
E10	22	SKJOTH F/AU
E11	4	SKJOTH FLEMMING/AU
E12	4	SKJOTH L/AU

=> s e1-e5 and tuberculosis

L4 31 ("SKJOT R L"/AU OR "SKJOT R L V"/AU OR "SKJOT RIKKE"/AU OR "SKJO  
T RIKKE L V"/AU OR "SKJOT RIKKE LOUISE VINTHER"/AU) AND TUBERCUL  
OSIS

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 11 DUP REM L4 (20 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 2004:59568 CAPLUS

DN 140:127185

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis**  
diagnosis and treatment

IN Andersen, Peter; **Skjot, Rikke Louise Vinther**; Okkels, Li Mei  
Meng; Brock, Inger; Oettinger, Thomas

PA Den.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----					
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FR, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		

DK 1997-376 A 19970402  
US 1997-44624P P 19970418  
EP 1998-913536 A3 19980401  
US 1999-289388 B2 19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; **Skjot, Rikke Louise Vinther**; Rasmussen, Peter Birk

PA Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

AN 2003:609858 CAPLUS

DN 139:163576

TI *Mycobacterium tuberculosis* antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

IN Andersen, Peter; **Skjot, Rikke Louise Vinther**

PA Den.

SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388,

abandoned.

CODEN: USXXCO

DT Patent

LA English

FAN. CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP	1508339	A1	20050223	EP 2004-77505	19940701
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
	US 5955077	A	19990921	US 1995-465640	19950605
EP	1449922	A2	20040825	EP 2004-76605	19980401
EP	1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1999-289388	B2	19990412		
	EP 1994-919574	A3	19940701		
	EP 1998-913536	A3	19980401		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

L5 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

AN 2002:906996 CAPLUS

DN 138:13499

TI Hybrids of M. **tuberculosis** antigens used as vaccines

IN Andersen, Peter; Olsen, Anja Weinreich; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk

PA Den.

SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 246,191, abandoned.

CODEN: USXXCO

DT Patent

LA English

FAN. CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002176867	A1	20021128	US 2001-805427	20010313
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI, CY

PRAI US 1997-44624P P 19970418  
DK 1997-1277 A 19971110  
US 1998-70488P P 19980105  
US 1998-246191 B2 19981230  
DK 1997-376 A 19970402  
EP 1998-913536 A3 19980401

AB The invention discloses fusion proteins consisting of T cell epitopes derived from the immunodominant antigens ESAT-6 and Ag85B from *Mycobacterium tuberculosis* or homologs thereof, and a *tuberculosis* vaccine based on the fusion proteins, which induces efficient immunol. memory. It is preferred that the sequences of the first and second T cell epitopes each have a sequence identity of at least 70% with the natively occurring sequence in the proteins from which they are derived. In the most preferred embodiment, the fusion polypeptide comprises ESAT-6 fused to Ag85B wherein ESAT-6 is fused to the C terminus of Ag85B. In one embodiment, there are nitric oxide linkers introduced between the 2 amino acid sequences constituting the parent polypeptide fragments.

L5 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 5

AN 2002:559608 BIOSIS

DN PREV200200559608

TI Epitope mapping of the immunodominant antigen TB10.4 and the two homologous proteins TB10.3 and TB12.9, which constitute a subfamily of the *esat-6* gene family.

AU **Skjot, Rikke Louise Vinther**; Brock, Inger; Arend, Sandra M.; Munk, Martin E.; Theisen, Michael; Ottenhoff, Tom H. M.; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark  
pa@ssi.dk

SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5446-5453.  
print.

CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 30 Oct 2002

Last Updated on STN: 30 Oct 2002

AB The human T-cell recognition of the low-molecular-mass culture filtrate antigen TB10.4 was evaluated in detail. The molecule was strongly recognized by T cells isolated from *tuberculosis* (TB) patients and from BCG-vaccinated donors. The epitopes on TB10.4 were mapped with overlapping peptides and found to be distributed throughout the molecule. The broadest response was found in TB patients, whereas the response in BCG-vaccinated donors was focused mainly toward a dominant epitope located in the N terminus (amino acids 1 to 18). The gene encoding TB10.4 was found to belong to a subfamily within the *esat-6* family that consists of the three highly homologous proteins TB10.4, TB10.3, and TB12.9 (Rv0288, Rv3019c, and Rv3017c, respectively). Southern blot analysis combined with database searches revealed that the three members of the TB10.4 family were present only in strains of the *Mycobacterium tuberculosis* complex, including BCG, and *M. kansasii*, whereas other atypical mycobacteria had either one (*M. avium*, *M. intracellulare*, and *M. marinum*) or none (*M. scrofulaceum*, *M. fortuitum*, and *M. szulgai*) of the genes. The fine specificity of the T-cell response to the three closely related *esat-6* family members was markedly different, with only a few epitopes shared between the molecules. Minimal differences in the amino acid sequence translated into large differences in recognition by T cells and secretion of gamma interferon. In general, the peptides from TB10.4 stimulated the largest responses, but epitopes unique to both TB10.3 and TB12.9 were found. The relevance of the findings for TB vaccine development and as a potential mechanism for immune evasion is discussed.

L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:50676 CAPLUS

DN 134:114829.  
 TI **Tuberculosis** vaccine and diagnostics based on the Mycobacterium  
**tuberculosis** esat-6 gene family  
 IN Andersen, Peter; Skjot, Rikke  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 80 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KR, KZ, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2378763	AA	20010118	CA 2000-2378763	20000713
	EP 1200466	A2	20020502	EP 2000-945660	20000713
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
	JP 2003510018	T2	20030318	JP 2001-509760	20000713
	AU 779495	B2	20050127	AU 2000-59664	20000713
	US 2004013685	A1	20040122	US 2001-872505	20010601

PRAI DK 1999-1020 A 19990713  
 US 1999-144011P P 19990715  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 US 1998-246191 B2 19981230  
 US 2000-615947 A2 20000713  
 WO 2000-DK398 W 20000713  
 US 2001-804980 A2 20010313

AB The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of Mycobacterium **tuberculosis**.

L5 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 DUPLICATE 6

AN 2001:534626 BIOSIS

DN PREV200100534626

TI Antigen discovery and **tuberculosis** vaccine development in the post-genomic era.

AU Skjot, Rikke Louise Vinther; Agger, Else Marie; Andersen, Peter  
 [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark

SO Scandinavian Journal of Infectious Diseases, (2001) Vol. 33, No. 9, pp. 643-647. print.

CODEN: SJIDB7. ISSN: 0036-5548.

DT Article

LA English

ED Entered STN: 14 Nov 2001

Last Updated on STN: 23 Feb 2002

AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against **tuberculosis**. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the Mycobacterium **tuberculosis** genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing

properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 AN 2003:208455 BIOSIS  
 DN PREV200300208455  
 TI Antigen discovery and **tuberculosis** vaccine development in the post-genomic era.  
 AU **Skjot, Rikke Louise Vinther**; Agger, Else Marie; Andersen, Peter [Reprint Author]  
 CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark  
 SO Scandinavian Journal of Infectious Diseases, (2001) No. Special Issue, pp. 79-83. print.  
 CODEN: SJIDB7. ISSN: 0036-5548.  
 DT Article  
 General Review; (Literature Review)  
 LA English  
 ED Entered STN: 30 Apr 2003  
 Last Updated on STN: 30 Apr 2003  
 AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against **tuberculosis**. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the Mycobacterium **tuberculosis** genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2000:260319 CAPLUS  
 DN 132:292711  
 TI Tb vaccine and diagnostic based on antigens from the Mycobacterium **tuberculosis** cell  
 IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; **Skjot, Rikke Louise Vinther**; Rosenkrands, Ida  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 126 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021983	A2	20000420	WO 1999-DK538	19991008
	WO 2000021983	A3	20001123		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2346218	AA	20000420	CA 1999-2346218	19991008

PRAI	DK 1998-1281	A	19981008
	US 1999-116673P	P	19990121
	WO 1999-DK538	W	19991008

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent Mycobacterium. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L5 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 7

AN 2000:349404 BIOSIS

DN PREV200000349404

TI Detection of active **tuberculosis** infection by T cell responses to early-secreted antigenic target 6-kDa protein and culture filtrate protein 10.

AU Arend, Sandra M. [Reprint author]; Andersen, Peter; van Meijgaarden, Krista E.; **Skjot, Rikke L. V.**; Subronto, Yanri W.; van Dissel, Jaap T.; Ottenhoff, Tom H. M.

CS Dept. of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden, Netherlands

SO Journal of Infectious Diseases, (May, 2000) Vol. 181, No. 5, pp. 1850-1854. print.

CODEN: JIDIAO. ISSN: 0022-1899.

DT Article

LA English

ED Entered STN: 16 Aug 2000

Last Updated on STN: 7 Jan 2002

AB The purified protein derivative (PPD) skin test has no predictive value for **tuberculosis** (TB) in *Mycobacterium bovis* bacillus Calmette-Guerin (BCG)-vaccinated individuals because of cross-reactive responses to nonspecific constituents of PPD. T cell responses to early-secreted antigenic target 6-kDa protein (ESAT-6) and the newly identified culture filtrate protein 10 (CFP-10), 2 proteins specifically expressed by *M. tuberculosis* (MTB) but not by BCG strains, were evaluated. Most TB patients responded to ESAT-6 (92%) or CFP-10 (89%). A minority of BCG-vaccinated individuals responded to both ESAT-6 and CFP-10, their history being consistent with latent infection with MTB in the presence of protective immunity. No responses were found in PPD-negative controls. The sensitivity and specificity of the assay were 84% and 100%, respectively, at a cutoff of 300 pg of interferon-gamma/mL. These data indicate that ESAT-6 and CFP-10 are promising antigens for highly specific immunodiagnosis of TB, even in BCG-vaccinated individuals.

L5 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 8

AN 2000:104643 BIOSIS

DN PREV200000104643

TI Comparative evaluation of low-molecular-mass proteins from *Mycobacterium tuberculosis* identifies members of the ESAT-6 family as immunodominant T-cell antigens.

AU **Skjot, Rikke Louise Vinther**; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen S, Denmark

SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.

DT Article

LA English

ED Entered STN: 22 Mar 2000

Last Updated on STN: 3 Jan 2002

AB Culture filtrate from *Mycobacterium tuberculosis* contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized *M. tuberculosis* proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. *Microbiology* 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in *Escherichia coli*, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human *tuberculosis* (TB) patients, *Mycobacterium bovis* BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

=&gt; e okkels li mei/au

E1	1	OKKELS JESPER/AU
E2	30	OKKELS L M/AU
E3	0 -->	OKKELS LI MEI/AU
E4	6	OKKELS LI MEI MENG/AU
E5	4	OKKELS LIMEI M/AU
E6	22	OKKELS LIMEI MENG/AU
E7	2	OKKELS S/AU
E8	4	OKKELS SIGURD/AU
E9	1	OKKELS THYGE FINN/AU
E10	1	OKKEMA A/AU
E11	4	OKKEMA A T/AU
E12	40	OKKEMA A Z/AU

=&gt; s e2-e6 and tuberculosis

L6 55 ("OKKELS L M"/AU OR "OKKELS LI MEI"/AU OR "OKKELS LI MEI MENG"/AU OR "OKKELS LIMEI M"/AU OR "OKKELS LIMEI MENG"/AU) AND TUBERCULOSIS

=&gt; dup rem l6

PROCESSING COMPLETED FOR L6

L7 13 DUP REM L6 (42 DUPLICATES REMOVED)

=&gt; d bib ab 1-

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 2005:119461 CAPLUS

DN 142:334537

TI Assessing the serodiagnostic potential of 35 *Mycobacterium tuberculosis* proteins and identification of four novel serological antigens

AU Weldingh, Karin; Rosenkrands, Ida; Okkels, Limei Meng; Doherty, T. Mark; Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut, Copenhagen, Den.

SO Journal of Clinical Microbiology (2005), 43(1), 57-65

CODEN: JCMIDW; ISSN: 0095-1137

PB American Society for Microbiology

DT Journal

LA English

AB Improved diagnostic reagents are needed for the detection of Mycobacterium tuberculosis infections, and the development of a serodiagnostic test would complement presently available diagnostic methods. The aim of the present study was to identify novel serol. targets for use for the future serodiagnosis of tuberculosis (TB). The authors cloned and expressed 35 M. tuberculosis proteins as recombinant proteins in Escherichia coli and analyzed their serodiagnostic potentials. By a two-step selection process, four superior seroantigens, TB9.7, TB15.3, TB16.3, and TB51, were identified, none of which has been described before. The four novel antigens were tested with panels of sera from smear-pos. and smear-neg. TB patients from areas both where TB is endemic and where TB is not endemic, with recognition frequencies ranging from 31 to 93% and with a specificity of at least 97%. The single most potent antigen was TB16.3, which had a sensitivity of 48 to 55% with samples from Danish resident TB patients and a sensitivity of 88 to 98% with samples from African TB patients. Importantly, the TB16.3 and the TB9.7 antigens were recognized by more than 85% of the samples from TB patients coinfecting with human immunodeficiency virus, a patient group for which it is in general difficult to detect M. tuberculosis -specific antibodies.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

AN 2004:59568 CAPLUS

DN 140:127185

TI Antigens from Mycobacterium as vaccine and uses in tuberculosis diagnosis and treatment

IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng  
; Brock, Inger; Oettinger, Thomas

PA Den.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		

US 2001-804980	A2	20010313
DK 1993-798	A	19930702
US 1993-123182	B2	19930920
WO 1994-DK273	A2	19940701
US 1995-465640	A1	19950605
DK 1997-376	A	19970402
US 1997-44624P	P	19970418
EP 1998-913536	A3	19980401
US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

L7 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 3

AN 2005:31533 BIOSIS

DN PREV200500031352

TI Protective effect of a **tuberculosis** subunit vaccine based on a fusion of antigen 85B and ESAT-6 in the aerosol guinea pig model.

AU Olsen, Anja W.; Williams, Ann; Okkels, Limei M.; Hatch, Graham; Andersen, Peter [Reprint Author]

CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
pa@ssi.dk

SO Infection and Immunity, (October 2004) Vol. 72, No. 10, pp. 6148-6150. print.

ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 12 Jan 2005

Last Updated on STN: 12 Jan 2005

AB A fusion protein of antigen 85B (Ag85B) and ESAT-6 administered in cationic lipid vesicles conferred a highly significant level of protection against *Mycobacterium tuberculosis* in the guinea pig aerosol model of infection. The protection was manifested as delayed clinical illness and prolonged survival. Neither Ag85B nor ESAT-6 (independently or as a cocktail) induced significant protection in this model.

L7 ANSWER 4 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 4

AN 2005:26452 BIOSIS

DN PREV200500027841

TI CFP10 discriminates between nonacetylated and acetylated ESAT-6 of *Mycobacterium tuberculosis* by differential interaction.

AU Okkels, Limei Meng; Mueller, Eva-Christina; Schmid, Monika; Rosenkrands, Ida; Kaufmann, Stefan H. E.; Andersen, Peter; Jungblut, Peter R. [Reprint Author]

CS Core Facil Prot Anal, Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany  
jungblut@mpiib-berlin.mpg.de

SO Proteomics, (October 2004) Vol. 4, No. 10, pp. 2954-2960. print.  
ISSN: 1615-9853 (ISSN print).

DT Article

LA English

ED Entered STN: 5 Jan 2005

Last Updated on STN: 5 Jan 2005

AB ESAT-6 (the 6 kDa early secreted antigenic target) protein species in short-term culture filtrate of *Mycobacterium tuberculosis* were separated in a 4-5 narrow range p/ gradient two-dimensional gel electrophoresis (2-DE). Eight ESAT-6 protein species were analyzed in detail by peptide mass fingerprinting matrix-assisted laser desorption/ionization-mass spectrometry as well as by electrospray

ionization-tandem mass spectrometry. An N-terminal Thr acetylation was identified in four species and a C-terminal truncation was identified in two species. In 2-DE blot overlay assays, the recombinant 10 kDa culture filtrate protein (CFP10) discriminated N-terminal acetylated and nonacetylated ESAT-6 by differential interaction, whereas removal of the C-terminal 11 residues of ESAT-6 had no effects thereon. This example shows that the access to the protein species level can be a prerequisite to understand regulation of protein-protein interaction.

L7 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 5  
AN 2004:307035 BIOSIS  
DN PREV200400304119  
TI Protein-protein interactions of proteins from the ESAT-6 family of  
Mycobacterium **tuberculosis**.  
AU **Okkels, Limei Meng** [Reprint Author]; Andersen, Peter  
CS Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany  
okkels@mpiib-berlin.mpg.de  
SO Journal of Bacteriology, (April 2004) Vol. 186, No. 8, pp. 2487-2491.  
print.  
CODEN: JOBAAY. ISSN: 0021-9193.  
DT Article  
LA English  
ED Entered STN: 7 Jul 2004  
Last Updated on STN: 7 Jul 2004  
AB In the present study, we demonstrate that, in analogy with the genes  
encoding ESAT-6 and CFP-10, the genes rv0287 and rv0288 from the ESAT-6  
gene family are cotranscribed. Using Western-Western blotting and  
protein-print overlay methodologies, we demonstrate that ESAT-6 and  
CFP-10, as well as the protein pair Rv0288/Rv0287, interact pairwise in a  
highly specific way. Most notably, the ESAT-6 proteins interact directly  
with Rv3873, a possible cell envelope component of the ESAT-6 secretion  
pathway.

L7 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6  
AN 2003:696302 CAPLUS  
DN 139:229237  
TI Protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment  
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio,  
Walter; **Okkels, Li Mei Meng**; Skjot, Rikke Louise Vinther;  
Rasmussen, Peter Birk  
PA Den.  
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		
AB	The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21,				

Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing *tuberculosis* caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating *tuberculosis* using antigens isolated from *Mycobacterium tuberculosis*.

L7 ANSWER 7 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 7

AN 2004:33002 BIOSIS

DN PREV200400035432

TI PPE protein (Rv3873) from DNA segment RD1 of *Mycobacterium tuberculosis*: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.

AU Okkels, Limei Meng [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark  
lmo@ssi.dk

SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123.  
print.

ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 7 Jan 2004

Last Updated on STN: 7 Jan 2004

AB Proteins encoded by DNA segment RD1 of *Mycobacterium tuberculosis* have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6), and the 10-kDa culture filtrate protein (CFP10), which are encoded by the *esx-lhp* operon in this region. In the present study we characterized a third putative open reading frame in this region, *rv3873*, which encodes a PPE protein. We found that the *rv3873* gene is expressed in *M. tuberculosis* H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from *tuberculosis* (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other RD1-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of *Mycobacterium bovis* BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated donors. The immunodominant epitope (residues 118 to 135) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.

L7 ANSWER 8 OF 13 CABA COPYRIGHT 2005 CABI on STN DUPLICATE 8

AN 2003:177804 CABA

DN 20033152549

TI Genomic approach to identification of *Mycobacterium bovis* diagnostic antigens in cattle

AU Aagaard, C.; Govaerts, M.; Okkels, L. M.; Andersen, P.; Pollock, J. M.

CS Department of Infectious Disease Immunology, Statens Serum Institute, Artillerivej 5, DK-2300 Copenhagen, Denmark. caa@ssi.dk

SO Journal of Clinical Microbiology, (2003) Vol. 41, No. 8, pp. 3719-3728. 46  
ref.

Publisher: American Society for Microbiology (ASM). Washington

ISSN: 0095-1137

DOI: 10.1128/JCM.41.8.3719-3728.2003

CY United States

DT Journal

LA English

ED Entered STN: 20031107

Last Updated on STN: 20031107

AB Differential delayed-type hypersensitivity skin testing with tuberculin purified protein derivatives from *Mycobacterium bovis* and *M. avium* is the standard for diagnosing bovine **tuberculosis**. However, improved tests based on defined, specific antigens are urgently needed. In the present study, a combination of bioinformatics, molecular biology, and bovine models of infection were used to screen mycobacterial proteins for their potential as diagnostic reagents which could be used in a whole-blood assay for diagnosis of **tuberculosis**. Initial screening of 28 proteins selected in silico and expressed as recombinants in *Escherichia coli* indicated that CFP-10, ESAT-6, TB27.4, TB16.2, TB15.8, and TB10.4 induced strong gamma interferon responses in experimentally infected cattle. A more thorough investigation over time in two groups of animals infected with a high (106 CFU) and a low (104 CFU) dose of *M. bovis* revealed that, for both groups, the strength of the in vitro response to individual antigens varied greatly over time. However, combining the results for ESAT-6, CFP-10, and TB27.4, possibly supplemented with TB10.4, gave sensitivities at different infection stages close to those obtained with *M. bovis* purified protein derivative. Importantly, while responsiveness to ESAT-6 and CFP-10 correlated strongly for individual samples, the same was not the case for ESAT-6 and TB27.4 responsiveness. The results suggest that combinations of specific antigens such as these have great potential in development of optimized diagnostic systems for bovine **tuberculosis**.

L7 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 9

AN 2004:76163 BIOSIS

DN PREV200400078267

TI Human T-cell responses to the RD1-encoded protein TB27.4 (Rv3878) from *Mycobacterium tuberculosis*.

AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei  
Meng; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.;  
Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
eag@ssi.dk

SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.  
CODEN: IMMUAM. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 4 Feb 2004

Last Updated on STN: 4 Feb 2004

AB In recent years, there has been considerable focus on the discovery and characterization of proteins derived from *Mycobacterium tuberculosis* leading to the identification of a number of candidate antigens for use in vaccine development or for diagnostic purposes. Previous experiments have demonstrated an important immunological role for proteins encoded by the RD1 region, which is absent from all strains of *Bacillus Calmette-Guerin* (BCG) but present in the genomes of virulent *M. bovis* and *M. tuberculosis*. Herein, we have studied human T-cell responses to the antigen encoded by the putative open reading frame (rv3878) of the RD1 region. Immunoblot analysis revealed that rv3878 was expressed and the native protein was designated TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a prominent immune response in human **tuberculosis** patients with a dominant region in the C-terminal part of the molecule. In contrast, very limited responses were seen in *M. bovis* BCG-vaccinated donors. This study therefore emphasizes the diagnostic potential of proteins encoded by the RD1 region.

L7 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 10

AN 2003:153335 BIOSIS

DN PREV200300153335  
 TI Selecting the components for a safe and efficient **tuberculosis** subunit vaccine: Recent progress and post-genomic insights.  
 AU **Okkels, Limei Meng**; Doherty, T. Mark; Andersen, Peter [Reprint Author]  
 CS Department of Infectious Disease Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen, Denmark  
 pa@ssi.dk  
 SO Current Pharmaceutical Biotechnology, (February 2003) Vol. 4, No. 1, pp. 69-83. print.  
 ISSN: 1389-2010 (ISSN print).  
 DT Article  
 General Review; (Literature Review)  
 LA English  
 ED Entered STN: 19 Mar 2003  
 Last Updated on STN: 19 Mar 2003

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:780953 CAPLUS  
 DN 135:343273  
 TI Cloning and immunogenicity of Mycobacterium **tuberculosis** proteins  
 IN Agger, Else Marie; Andersen, Peter; **Okkels, Li Mei Meng**; Weldingh, Karin  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 111 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079274	A2	20011025	WO 2001-DK276	20010419
	WO 2001079274	A3	20020711		
	WO 2001079274	B1	20020808		
	WO 2001079274	C1	20040429		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2405247	AA	20011025	CA 2001-2405247	20010419
	EP 1278769	A2	20030129	EP 2001-923542	20010419
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
PRAI	DK 2000-666	A	20000419		
	DK 2001-283	A	20010221		
	WO 2001-DK276	W	20010419		

AB The authors disclose the identification and characterization of a number of novel Mycobacterium **tuberculosis** derived proteins and protein fragments. The proteins and protein fragments were examined for their ability to elicit interferon- $\gamma$  production and/or a T-cell proliferative response in guinea pigs and humans with **tuberculosis**.

L7 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
 AN 2001:302988 BIOSIS  
 DN PREV200100302988  
 TI Protection of mice with a **tuberculosis** subunit vaccine based on a fusion protein of antigen 85B and ESAT-6.  
 AU Olsen, Anja Weinreich; van Pinxteren, Laurens A. H.; **Okkels, Limei Meng**; Rasmussen, Peter Birk; Andersen, Peter [Reprint author]  
 CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,

DK-2300, Copenhagen S, Denmark  
 pa@ssi.dk  
 SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 2773-2778. print.  
 CODEN: INFIBR. ISSN: 0019-9567.  
 DT Article  
 LA English  
 ED Entered STN: 27 Jun 2001  
 Last Updated on STN: 19 Feb 2002  
 AB In this study, we investigated the potential of a **tuberculosis** subunit vaccine based on fusion proteins of the immunodominant antigens ESAT-6 and antigen 85B. When the fusion proteins were administered to mice in the adjuvant combination dimethyl dioctadecylammonium bromide-monophosphoryl lipid A, a strong dose-dependent immune response was induced to both single components as well as to the fusion proteins. The immune response induced was accompanied by high levels of protective immunity and reached the level of Mycobacterium bovis BCG-induced protection over a broad dose range. The vaccine induced efficient immunological memory, which remained stable 30 weeks postvaccination.

L7 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:260319 CAPLUS

DN 132:292711

TI Tb vaccine and diagnostic based on antigens from the Mycobacterium **tuberculosis** cell

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; **Okkels, Li Mei Meng**; Skjot, Rikke Louise Vinther; Rosenkrands, Ida

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021983	A2	20000420	WO 1999-DK538	19991008
	WO 2000021983	A3	20001123		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2346218	AA	20000420	CA 1999-2346218	19991008
	AU 9960784	A1	20000501	AU 1999-60784	19991008
	AU 766093	B2	20031009		
	EP 1117683	A2	20010725	EP 1999-947257	19991008
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO			
PRAI	DK 1998-1281	A	19981008		
	US 1999-116673P	P	19990121		
	WO 1999-DK538	W	19991008		

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent Mycobacterium. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

=> e brock inger/au

E1	1	BROCK III T O/AU
E2	1	BROCK IINGER/AU
E3	27 -->	BROCK INGER/AU
E4	2	BROCK IRVIN R/AU
E5	2	BROCK IV ROBERT C/AU
E6	1	BROCK IVAN H/AU
E7	1	BROCK IVAN HEINZ/AU
E8	1	BROCK IVAN R/AU
E9	943	BROCK J/AU
E10	1	BROCK J */AU
E11	360	BROCK J A/AU
E12	8	BROCK J A C/AU

=> s e3 and tuberculosis

L8 25 "BROCK INGER"/AU AND TUBERCULOSIS

=> dup rem l8

PROCESSING COMPLETED FOR L8

L9 11 DUP REM L8 (14 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 2004:59568 CAPLUS

DN 140:127185

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis**  
diagnosis and treatment

IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng;  
**Brock, Inger**; Oettinger, Thomas

PA Den.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		

US 1995-465640	A1	19950605
DK 1997-376	A	19970402
US 1997-44624P	P	19970418
EP 1998-913536	A3	19980401
US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium **tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from Mycobacterium **tuberculosis**.

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:996402 CAPLUS

DN 141:423306

TI Compositions comprising multiple T cell epitopes of mycobacterial antigens for immunodiagnosis and immunotherapy of **tuberculosis**

IN Andersen, Peter; Brock, Inger; Weldingh, Karin

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004099771	A1	20041118	WO 2004-DK314	20040506
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
	AZ, BY, KG, KZ, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				
	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				
	SN, TD, TG				

PRAI DK 2003-699 A 20030508

AB The current used method for immunol. diagnosis of **tuberculosis** infection, the tuberculin skin test, is problematic for a number of reasons; it has low specificity in BCG vaccinated individuals, a high interobserver variance and requires skill to be read and interpreted. Furthermore it requires an extra visit to the clinic to have the test read. Both people vaccinated with BCG and those exposed to non-**tuberculosis** mycobacteria give a pos. skin test result similar to that seen in a TB infected individual. This also applies for purified protein derivative (PPD) when used in a blood cell based test. The present invention disclosed the development of an immunol. TB diagnostic tool based on a combination of T cell epitopes from proteins encoded by regions of the M. **tuberculosis** genome, that are not present in the BCG vaccine strain or in the most common non-**tuberculosis** mycobacteria. Four recently characterized proteins (i.e. Rv2654, Rv2653, Rv3873 and Rv3878) with this diagnostic potential were selected. Peptides from these proteins were tested one by one with peripheral blood mononuclear cells from microscopy or culture confirmed TB patients as well as from healthy BCG vaccinated controls. Some combinations of peptides showed a sensitivity level comparable to the level seen with these peptides combined with ESAT 6 and CFP 10 gave a sensitivity of 93% representing a raise in sensitivity of about 26-33% compared to using ESAT6 or CFP10 alone. The results from a panel of TB patients, using a collection of the new specific epitopes clearly demonstrates, the addition of other specific epitopes to the already known specific antigens, increases the sensitivity of a diagnostic assay based on cell mediated immune response.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

- L9 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 2  
AN 2004:309660 BIOSIS  
DN PREV200400309678  
TI Healthy individuals that control a latent infection with Mycobacterium  
**tuberculosis** express high levels of Th1 cytokines and the IL-4  
antagonist IL-4delta2.  
AU Demissie, Abebech; Abebe, Markos; Aseffa, Abraham; Rook, Graham; Fletcher,  
Helen; Zumla, Alimuddin; Weldingh, Karin; **Brock, Inger**;  
Andersen, Peter; Doherty, T. Mark [Reprint Author]; VACSEL Study Group  
CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300,  
Copenhagen, S, Denmark  
TMD@ssi.dk  
SO Journal of Immunology, (June 1 2004) Vol. 172, No. 11, pp. 6938-6943.  
print.  
ISSN: 0022-1767 (ISSN print).  
DT Article  
LA English  
ED Entered STN: 7 Jul 2004  
Last Updated on STN: 7 Jul 2004  
AB The majority of healthy individuals exposed to Mycobacterium  
**tuberculosis** will not develop disease and identifying what  
constitutes "protective immunity" is one of the holy grails of M.  
**tuberculosis** immunology. It is known that IFN-gamma is essential  
for protection, but it is also apparent that IFN-gamma levels alone do not  
explain the immunity/susceptibility dichotomy. The controversy regarding  
correlates of immunity persists because identifying infected but healthy  
individuals (those who are immune) has been problematic. We have  
therefore used recognition of the M. **tuberculosis** virulence  
factor early secretory antigenic target 6 to identify healthy, but  
infected individuals from **tuberculosis** (TB)-endemic and  
nonendemic regions (Ethiopia and Denmark) and have compared signals for  
cytokines expressed directly ex vivo with the pattern found in TB  
patients. We find that TB patients are characterized by decreased levels  
of Th1 cytokines and increased levels of IL-10 compared with the healthy  
infected and noninfected community controls. Interestingly, the healthy  
infected subjects exhibited a selective increase of message for the IL-4  
antagonist, IL-4delta2, compared with both TB patients or noninfected  
individuals. These data suggest that long-term control of M.  
**tuberculosis** infection is associated not just with elevated Th1  
responses but also with inhibition of the Th2 response.
- L9 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3  
AN 2004:572566 CAPLUS  
DN 141:294300  
TI Specific T-cell epitopes for immunoassay-based diagnosis of Mycobacterium  
**tuberculosis** infection  
AU **Brock, Inger**; Weldingh, Karin; Leyten, Eliane M. S.; Arend,  
Sandra M.; Ravn, Pernille; Andersen, Peter  
CS Department of Infectious Disease Immunology, Statens Serum Institute,  
Copenhagen, Den.  
SO Journal of Clinical Microbiology (2004), 42(6), 2379-2387  
CODEN: JCMIDW; ISSN: 0095-1137  
PB American Society for Microbiology  
DT Journal  
LA English  
AB The currently used method for immunol. detection of **tuberculosis**  
infection, the tuberculin skin test, has low specificity. Antigens  
specific for Mycobacterium **tuberculosis** to replace purified  
protein derivative are therefore urgently needed. We have performed a  
rigorous assessment of the diagnostic potential of four recently  
identified antigens (Rv2653, Rv2654, Rv3873, and Rv3878) from genomic  
regions that are lacking from the Mycobacterium bovis bacillus  
Calmette-Guerin (BCG) vaccine strains as well as from the most common  
nontuberculous mycobacteria. The fine specificity of potential epitopes  
in these mols. was evaluated by sensitive testing of the T-cell responses

of peripheral blood mononuclear cells derived from M. bovis BCG-vaccinated healthy individuals to synthesized overlapping peptides. Three of the four mols. contained regions with significant specificity problems (Rv2653, Rv3873, and Rv3878). We selected and combined the specific peptide stretches from the four proteins not recognized by M. bovis BCG-vaccinated individuals. These peptide stretches were tested with peripheral blood mononuclear cells obtained from patients with microscopy-or culture-confirmed **tuberculosis** and from healthy M. bovis BCG-vaccinated controls. The combination of the most promising stretches from this anal. showed a sensitivity level (57%) comparable to the level found with the two well-known M. **tuberculosis**-specific proteins ESAT-6 and CFP-10 (75 and 66%, resp.). The combination of ESAT-6, CFP-10, and the novel specific peptide stretches gave an overall sensitivity of 84% at a specificity of 97%. In a validation experiment with new exptl. groups, the sensitivities obtained were 57% for the combination of peptides and 90% for the combination of the peptides, ESAT-6, and CFP-10. This combination gave a specificity of 95%.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 4

AN 2004:211482 BIOSIS

DN PREV200400213609

TI Mapping immune reactivity toward Rv2653 and Rv2654: Two novel  
low-molecular-mass antigens found specifically in the Mycobacterium  
**tuberculosis** complex.

AU Aagaard, Claus [Reprint Author]; **Brock, Inger**; Olsen, Anja;  
Ottenhoff, Tom H. M.; Weldingh, Karin; Andersen, Peter

CS Dept. of Infectious Disease Immunology, Statens Serum Institute,  
Artillerivej 5, DK-2300, Copenhagen, Denmark  
caa@ssi.dk

SO Journal of Infectious Diseases, (1 March 2004) Vol. 189, No. 5, pp.  
812-819. print.

CODEN: JIDIAQ. ISSN: 0022-1899.

DT Article

LA English

ED Entered STN: 14 Apr 2004

Last Updated on STN: 14 Apr 2004

AB New tools are urgently needed for the detection of latent  
**tuberculosis** (TB). We evaluated the diagnostic potential of 2  
novel Mycobacterium **tuberculosis** complex-specific candidate  
antigens (Rv2653 and Rv2654) and investigated T cell recognition during  
natural infection in humans and experimental infection in guinea pigs.  
Peripheral blood mononuclear cells stimulated with peptide pools covering  
the full length of Rv2654 induced interferon-gamma release in 10 of 19  
patients with TB. Neither Rv2654 single peptides nor Rv2654 pools were  
recognized by bacille Calmette-Guerin-vaccinated donors. However,  
peptides from Rv2653 were recognized by both patients group. The  
cross-reactive epitope(s) in Rv2653 were located in a 36-amino acid  
stretch in the center of the molecule. Rv2654 also induced M.  
**tuberculosis**-specific skin-test responses in 3 of 4  
aerosol-infected guinea pigs. Rv2654 is a strongly recognized T cell  
antigen that is highly specific for TB and has potential as a novel  
cell-mediated immunity-based TB diagnostic agent.

L9 ANSWER 6 OF 11 MEDLINE on STN

AN 2004317793 MEDLINE

DN PubMed ID: 15087297

TI Comparison of tuberculin skin test and new specific blood test in  
**tuberculosis** contacts.

CM Comment in: Am J Respir Crit Care Med. 2004 Jul 1;170(1):5-6. PubMed ID:  
15220119

AU **Brock Inger**; Weldingh Karin; Lillebaek Troels; Follmann Frank;  
Andersen Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300 Copenhagen S, Denmark.

SO American journal of respiratory and critical care medicine, (2004 Jul 1)

170 (1) 65-9. Electronic Publication: 2004-04-15.

Journal code: 9421642. ISSN: 1073-449X.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200408

ED Entered STN: 20040629

Last Updated on STN: 20040806

Entered Medline: 20040805

AB The tuberculin skin test used to detect latent *Mycobacterium tuberculosis* infection has many drawbacks, and a new diagnostic test for latent *tuberculosis* (Quantiferon-TB [QFT-TB]) has recently been introduced. This test measures the production of IFN-gamma in whole blood upon stimulation with purified protein derivative (PPD). The QFT-TB test addresses the operational problems with the tuberculin skin test, but, as the test is based on PPD, it still has a low specificity in populations vaccinated with the Bacille Calmette-Guerin (BCG) vaccine. We have modified the test to include the antigens ESAT-6 and CFP-10, which are not present in BCG vaccine strains or the vast majority of nontuberculous mycobacteria. This test was used to detect infection in contacts in a *tuberculosis* outbreak at a Danish high school. The majority of the contacts were BCG-unvaccinated, which allowed a direct comparison of the skin test and the novel blood test in individuals whose skin test was not confounded by vaccination. An excellent agreement between the two tests was found (94%, kappa value 0.866), and in contrast to the blood test based on PPD, the novel blood test was not influenced by the vaccination status of the subjects tested.

L9 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 5

AN 2004:33002 BIOSIS

DN PREV200400035432

TI PPE protein (Rv3873) from DNA segment RD1 of *Mycobacterium tuberculosis*: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.

AU Okkels, Limei Meng [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark  
lmo@ssi.dk

SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123.  
print.

ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 7 Jan 2004

Last Updated on STN: 7 Jan 2004

AB Proteins encoded by DNA segment RD1 of *Mycobacterium tuberculosis* have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6), and the 10-kDa culture filtrate protein (CFP10), which are encoded by the *esx-lhp* operon in this region. In the present study we characterized a third putative open reading frame in this region, *rv3873*, which encodes a PPE protein. We found that the *rv3873* gene is expressed in *M. tuberculosis* H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from *tuberculosis* (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other RD1-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of *Mycobacterium bovis* BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated

donors. The immunodominant epitope (residues 118 to 135) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.

- L9 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 6
- AN 2004:76163 BIOSIS
- DN PREV200400078267
- TI Human T-cell responses to the RD1-encoded protein TB27.4 (Rv3878) from  
*Mycobacterium tuberculosis*.
- AU Agger, Else Marie [Reprint Author]; **Brock, Inger**; Okkels, Limei  
Meng; Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.; Andersen,  
Peter
- CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
eag@ssi.dk
- SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.  
CODEN: IMMUAM. ISSN: 0019-2805.
- DT Article
- LA English
- ED Entered STN: 4 Feb 2004  
Last Updated on STN: 4 Feb 2004
- AB In recent years, there has been considerable focus on the discovery and  
characterization of proteins derived from *Mycobacterium  
tuberculosis* leading to the identification of a number of  
candidate antigens for use in vaccine development or for diagnostic  
purposes. Previous experiments have demonstrated an important  
immunological role for proteins encoded by the RD1 region, which is absent  
from all strains of bacillus Calmette-Guerin (BCG) but present in the  
genomes of virulent *M. bovis* and *M. tuberculosis*. Herein, we  
have studied human T-cell responses to the antigen encoded by the putative  
open reading frame (rv3878) of the RD1 region. Immunoblot analysis  
revealed that rv3878 was expressed and the native protein was designated  
TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a  
prominent immune response in human *tuberculosis* patients with a  
dominant region in the C-terminal part of the molecule. In contrast, very  
limited responses were seen in *M. bovis* BCG-vaccinated donors. This study  
therefore emphasizes the diagnostic potential of proteins encoded by the  
RD1 region.
- L9 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 7
- AN 2002:559608 BIOSIS
- DN PREV200200559608
- TI Epitope mapping of the immunodominant antigen TB10.4 and the two  
homologous proteins TB10.3 and TB12.9, which constitute a subfamily of the  
esat-6 gene family.
- AU Skjot, Rikke Louise Vinther; **Brock, Inger**; Arend, Sandra M.;  
Munk, Martin E.; Theisen, Michael; Ottenhoff, Tom H. M.; Andersen, Peter  
[Reprint author]
- CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen S, Denmark  
pa@ssi.dk
- SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5446-5453.  
print.  
CODEN: INFIBR. ISSN: 0019-9567.
- DT Article
- LA English
- ED Entered STN: 30 Oct 2002  
Last Updated on STN: 30 Oct 2002
- AB The human T-cell recognition of the low-molecular-mass culture filtrate  
antigen TB10.4 was evaluated in detail. The molecule was strongly  
recognized by T cells isolated from *tuberculosis* (TB) patients  
and from BCG-vaccinated donors. The epitopes on TB10.4 were mapped with  
overlapping peptides and found to be distributed throughout the molecule.  
The broadest response was found in TB patients, whereas the response in  
BCG-vaccinated donors was focused mainly toward a dominant epitope located  
in the N terminus (amino acids 1 to 18). The gene encoding TB10.4 was

found to belong to a subfamily within the esat-6 family that consists of the three highly homologous proteins TB10.4, TB10.3, and TB12.9 (Rv0288, Rv3019c, and Rv3017c, respectively). Southern blot analysis combined with database searches revealed that the three members of the TB10.4 family were present only in strains of the *Mycobacterium tuberculosis* complex, including BCG, and *M. kansasii*, whereas other atypical mycobacteria had either one (*M. avium*, *M. intracellulare*, and *M. marinum*) or none (*M. scrofulaceum*, *M. fortuitum*, and *M. szulgai*) of the genes. The fine specificity of the T-cell response to the three closely related esat-6 family members was markedly different, with only a few epitopes shared between the molecules. Minimal differences in the amino acid sequence translated into large differences in recognition by T cells and secretion of gamma interferon. In general, the peptides from TB10.4 stimulated the largest responses, but epitopes unique to both TB10.3 and TB12.9 were found. The relevance of the findings for TB vaccine development and as a potential mechanism for immune evasion is discussed.

- L9 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN  
AN 2001:94979 BIOSIS  
DN PREV200100094979  
TI Use of ESAT-6 and CFP-10 antigens for diagnosis of extrapulmonary  
**tuberculosis**.  
AU Munk, Martin E. [Reprint author]; Arend, Sandra M.; Brock, Inger  
; Ottenhoff, Tom H. M.; Andersen, Peter  
CS Dept. of Tuberculosis Immunology, States Serum Institute, 5, Artillerivej,  
2300, Copenhagen S, Denmark  
mmn@ssi.dk  
SO Journal of Infectious Diseases, (1 January, 2001) Vol. 183, No. 1, pp.  
175-176. print.  
CODEN: JIDIAQ. ISSN: 0022-1899.  
DT Letter  
LA English  
ED Entered STN: 21 Feb 2001  
Last Updated on STN: 15 Feb 2002
- L9 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN  
DUPLICATE 8  
AN 2000:104643 BIOSIS  
DN PREV200000104643  
TI Comparative evaluation of low-molecular-mass proteins from *Mycobacterium*  
**tuberculosis** identifies members of the ESAT-6 family as  
immunodominant T-cell antigens.  
AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn,  
Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter  
[Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen S, Denmark  
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002
- AB Culture filtrate from *Mycobacterium tuberculosis* contains  
protective antigens of relevance for the generation of a new  
antituberculosis vaccine. We have identified two previously  
uncharacterized *M. tuberculosis* proteins (TB7.3 and TB10.4) from  
the highly active low-mass fraction of culture filtrate. The molecules  
were characterized, mapped in a two-dimensional electrophoresis reference  
map of short-term culture filtrate, and compared with another recently  
identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I.  
Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203,  
1998), and the well-described ESAT-6 antigen. Genetic analyses  
demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of  
low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside  
this family. The proteins were expressed in *Escherichia coli*, and their  
immunogenicity was tested in cultures of peripheral blood mononuclear

cells from human **tuberculosis** (TB) patients, *Mycobacterium bovis* BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

=> e oettinger thomas/au

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E1      5      OETTINGER T P/AU
E2      2      OETTINGER TH/AU
E3     22 --> OETTINGER THOMAS/AU
E4      6      OETTINGER THOMAS P/AU
E5      7      OETTINGER U/AU
E6      2      OETTINGER ULRICH/AU
E7     171     OETTINGER W/AU
E8      1      OETTINGER W H/AU
E9      1      OETTINGER W K/AU
E10     2      OETTINGER W K E/AU
E11     1      OETTINGER W ROBERTO/AU
E12     67     OETTINGER WILLI/AU

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=> s e1-e4 and tuberculosis

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L10     24 ("OETTINGER T P"/AU OR "OETTINGER TH"/AU OR "OETTINGER THOMAS"/A
        U OR "OETTINGER THOMAS P"/AU) AND TUBERCULOSIS

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=> dup rem l10

PROCESSING COMPLETED FOR L10

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L11     13 DUP REM L10 (11 DUPLICATES REMOVED)

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=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

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L11 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

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AN 2004:490265 CAPLUS

DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN Andersen, Peter; Skiot, Rikke; **Oettinger, Thomas**; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

PA Den.

SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

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PRAI DK 1997-376      A      19970402

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      US 1997-44624P   P      19970418

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      DK 1997-1277     A      19971110

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      US 1998-70488P   P      19980105

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      US 1998-50739    A2     19980330

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      DK 1998-1281     A      19981008

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      EP 1998-913536   A3     19980401

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AB The present invention is based on the identification and characterization

of a number of M. **tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L11 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

AN 2004:59568 CAPLUS

DN 140:127185

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment

IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; **Oettinger, Thomas**

PA Den.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	EP 1998-913536	A3	19980401		
	US 1999-289388	B2	19990412		
AB	The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from Mycobacterium <b>tuberculosis</b> . The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing <b>tuberculosis</b> caused by virulent mycobacteria in an animal, including a human being. The invention related to treating <b>tuberculosis</b> using antigens isolated from Mycobacterium <b>tuberculosis</b> .				

L11 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 3  
AN 2004:5335 BIOSIS  
DN PREV200400007544  
TI Nucleic acids fragments and polypeptide fragments derived from M.  
**tuberculosis**.  
AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor];  
**Oettinger, Thomas** [Inventor]; Rasmussen, Peter Birk [Inventor];  
Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter  
[Inventor]  
CS Bronshoj, Denmark  
ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark  
PI US 6641814 20031104  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>.  
e-file.  
ISSN: 0098-1133 (ISSN print).  
DT Patent  
LA English  
ED Entered STN: 17 Dec 2003  
Last Updated on STN: 17 Dec 2003  
AB The present invention is based on the identification and characterization  
of a number of M. **tuberculosis** derived novel proteins and  
protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48,  
50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141,  
143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to  
the polypeptides and immunologically active fragments thereof, the genes  
encoding them, immunological compositions such as vaccines and skin test  
reagents containing the polypeptides. Another part of the invention is  
based on the surprising discovery that fusions between ESAT-6 and MPT59  
are superior immunogens compared to each of the unfused proteins,  
respectively.

L11 ANSWER 4 OF 13 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M.  
**tuberculosis**  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
**Oettinger, Thomas**, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention is based on the identification and  
characterization of a number of M. **tuberculosis** derived novel  
proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16,  
17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88,  
90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The  
invention is directed to the polypeptides and immunologically active  
fragments thereof, the genes encoding them, immunological compositions

such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L11 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 4  
AN 2001:222123 BIOSIS  
DN PREV200100222123  
TI Diagnostic skin test for **tuberculosis**.  
AU Haslov, Kaare [Inventor]; Andersen, Ase Bengaard [Inventor];  
**Oettinger, Thomas** [Inventor]  
PI US 6120776 20000919  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Sep. 19, 2000) Vol. 1238, No. 3. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DT Patent  
LA English  
ED Entered STN: 9 May 2001  
Last Updated on STN: 18 Feb 2002  
AB Diagnostic methods capable of discriminating between cell mediated  
immunologic responses due to on the one hand active **tuberculosis**  
caused by bacteria belonging to the **tuberculosis** complex  
(Mycobacterium **tuberculosis**, Mycobacterium africanum and  
Mycobacterium bovis) and on the other hand vaccination with an immunogenic  
agent conferring immunity to **tuberculosis**. A diagnostic kit is  
also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting  
a delayed type hypersensitivity reaction (Dth) in animals with active  
**tuberculosis**, but not in animals vaccinated against TB with an  
immunogenic agent (e.g. M. bovis BCG strain: Danish 1331). Also provided  
are polypeptide fragments comprising a T-cell epitope of MPT64 as well as  
nucleic acid fragments encoding these polypeptide fragments.

L11 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 5  
AN 2000:104643 BIOSIS  
DN PREV2000000104643  
TI Comparative evaluation of low-molecular-mass proteins from Mycobacterium  
**tuberculosis** identifies members of the ESAT-6 family as  
immunodominant T-cell antigens.  
AU Skjot, Rikke Louise Vinther; **Oettinger, Thomas**; Rosenkrands,  
Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter  
[Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen S, Denmark  
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002  
AB Culture filtrate from Mycobacterium **tuberculosis** contains  
protective antigens of relevance for the generation of a new  
antituberculosis vaccine. We have identified two previously  
uncharacterized M. **tuberculosis** proteins (TB7.3 and TB10.4) from  
the highly active low-mass fraction of culture filtrate. The molecules  
were characterized, mapped in a two-dimensional electrophoresis reference  
map of short-term culture filtrate, and compared with another recently  
identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I.  
Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203,  
1998), and the well-described ESAT-6 antigen. Genetic analyses  
demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of  
low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside  
this family. The proteins were expressed in Escherichia coli, and their  
immunogenicity was tested in cultures of peripheral blood mononuclear  
cells from human **tuberculosis** (TB) patients, Mycobacterium bovis  
BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family  
members, TB10.4 and CFP10, were very strongly recognized and induced gamma

interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

L11 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of Mycobacterium tuberculosis culture filtrates and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		

WO 1998-DK132            W        19980401  
EP 1998-947412        A3       19981008  
WO 1998-DK438            W       19981008

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a  $\lambda$ gt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9        THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN  
DUPLICATE 6

AN 1998:348514 BIOSIS

DN PREV199800348514

TI Delayed-type hypersensitivity responses to ESAT-6 and MPT64 from  
*Mycobacterium tuberculosis* in the guinea pig.

AU Elhay, Martin J.; Oettinger, Thomas; Andersen, Peter [Reprint  
author]

CS Dep. T.B. Immunol., Statens Serum Inst., Artillerivej 5, Copenhagen 2300,  
Denmark

SO Infection and Immunity, (July, 1998) Vol. 66, No. 7, pp. 3454-3456. print.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 13 Aug 1998

Last Updated on STN: 13 Aug 1998

AB Two antigens from *Mycobacterium tuberculosis*, ESAT-6 and MPT64, elicited delayed-type hypersensitivity (DTH) skin responses in outbred guinea pigs infected with *M. tuberculosis* by the aerosol and intravenous routes but not those sensitized with *M. bovis* BCG or *M. avium*. The DTH epitope of ESAT-6 was mapped to the C terminus. Nonresponders to the individual antigens were found, but all animals responded to a combination of ESAT-6 and MPT64 or their respective minimal target peptides. Correspondingly, these molecules could form the basis of a new skin test for *tuberculosis*.

L11 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:632476 CAPLUS

DN 125:325659

TI Key epitopes on the ESAT-6 antigen recognized in mice during the recall of protective immunity to *Mycobacterium tuberculosis*

AU Brandt, Lise; Oettinger, Thomas; Holm, Arne; Andersen, Aase B.;  
Andersen, Peter

CS Bacterial Vaccine and Mycobacteria Dep., Royal Veterinary and Agricultural  
Univ., Copenhagen, Den.

SO Journal of Immunology (1996), 157(8), 3527-3533  
CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

AB The recall of long-lived immunity in a mouse model of *tuberculosis* (TB) is defined as an accelerated accumulation of reactive T cells in the target organs. The authors have recently identified antigen (Ag) 85B and a 6-kDa early secretory antigenic target, designated ESAT-6, as key antigenic targets recognized by these cells. Here, preferential recognition of the ESAT-6 Ag during the recall of immunity was shared by 5 of 6 genetically different strains of mice. Overlapping peptides spanning the sequence of ESAT-6 were used to map 2 T cell epitopes on this mol. One epitope recognized in the context of H-2b,d was located in the N-terminal part of the mol., whereas an epitope recognized in the context of H-2a,k covered amino acids 51-60. Shorter versions of the N-terminal epitope allowed the precise definition of a 13-amino acid core sequence

recognized in the context of H-2b. The peptide covering the N-terminal epitope was immunogenic, and a T cell response with the same fine specificity as that induced during TB infection was generated by immunization with the peptide in IFA. In the C57BL/6j strain, this single epitope was recognized by an exceedingly high frequency of splenic T cells (.apprx.1:1000), representing 25-35% of the total culture filtrate-reactive T cells recruited to the site of infection during the first phase of the recall response. These findings emphasize the relevance of this Ag in the immune response to TB and suggest that immunol. recognition in the first phase of infection is a highly restricted event dominated by a limited number of T cell clones.

L11 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 7  
AN 1996:76919 BIOSIS  
DN PREV199698649054  
TI Evidence for occurrence of the ESAT-6 protein in Mycobacterium  
**tuberculosis** and virulent Mycobacterium bovis and for its absence  
in Mycobacterium bovis BCG.  
AU Harboe, Morten [Reprint author]; Oettinger, Thomas; Wiker,  
Harald Gotten; Rosenkrands, Ida; Andersen, Peter  
CS Inst. Immunol. Rheumatol., Univ. Oslo, N-0172 Oslo, Norway  
SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 16-22.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 27 Feb 1996  
Last Updated on STN: 27 Feb 1996  
AB ESAT-6 is a secreted protein present in the short-term culture filtrate of  
Mycobacterium **tuberculosis** after growth on a synthetic Sauton  
medium. ESAT-6 has recently been demonstrated to induce strong T-cell  
responses in a mouse model of memory immunity after infection with M.  
**tuberculosis**. In Western blotting (immunoblotting), the  
monoclonal antibody HYB76-8. reacting with ESAT-6, gave a 6-kDa band in  
culture filtrates from M. **tuberculosis** and virulent  
Mycobacterium bovis. A distinct band in the 24-kDa region was observed in  
filtrates from four of eight substrains of M. bovis BCG that produced high  
levels of MPB64, while no band occurred in the 6-kDa region with any of  
these BCG substrains. Southern blotting and PCR experiments with genomic  
mycobacterial DNA showed the presence of the esat-6 gene in reference  
strains and clinical isolates of V. **tuberculosis** as well as in  
virulent M. bovis. The esat-6 gene could not be demonstrated in any of  
the eight substrains of M. bovis BCG tested by these techniques. Two gene  
deletions that distinguish M. bovis BCG from virulently M. bovis have thus  
now been demonstrated. Deletion of mpb64 affects four of the eight  
substrains tested; deletion of esat-6 affects all of them. The reaction  
of HYB76-8 at 26 kDa with four of the BCG substrains was demonstrated to  
result from cross-reactivity with MPB64. HYB76-8 was also shown to  
cross-react with the A, B, and C components of the antigen 85 complex and  
MPT51.

L11 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1995:498385 CAPLUS  
DN 122:260539  
TI Diagnostic skin test for **tuberculosis**: a method able to  
distinguish infection from vaccination  
IN Hasloev, Kaare; Andersen, Aase Bengaard; Oettinger, Thomas  
PA Statens Seruminstitut, Den.  
SO PCT Int. Appl., 85 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9501440	A1	19950112	WO 1994-DK270	19940630
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK,				
	ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD,				

MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ,  
TT, UA

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9470686	A1	19950124	AU 1994-70686	19940630
AU 685133	B2	19980115		
EP 749486	A1	19961227	EP 1994-919572	19940630
R: BE, CH, DE, ES, FR, GB, IT, LI				
US 6120776	A	20000919	US 1996-569221	19960212
PRAI DK 1993-797	A	19930702		
WO 1994-DK270	W	19940630		

AB Diagnostic methods capable of discriminating between cell mediated immunol. responses due to on the one hand active **tuberculosis** caused by bacteria belonging to the **tuberculosis** complex (Mycobacterium **tuberculosis**, Mycobacterium africanum and Mycobacterium bovis) and on the other hand vaccination with an immunogenic agent conferring immunity to **tuberculosis**. A diagnostic kit is also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting a delayed type hypersensitivity reaction in animals with active **tuberculosis**, but not in animals vaccinated against TB with an immunogenic agent (e.g. M. bovis BCG strain: Danish 1331). Also provided are polypeptide fragments comprising a T-cell epitope of MPT64 as well as nucleic acid fragments encoding these polypeptide fragments.

L11 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 8

AN 1996:21932 BIOSIS

DN PREV199698594067

TI Mapping of the delayed-type hypersensitivity-inducing epitope of secreted protein MPT64 from Mycobacterium **tuberculosis**.

AU **Oettinger, Thomas** [Reprint author]; Holm, Arne; Mtoni, Isaac M.; Andersen, Ase B.; Haslov, Kaare

CS Mycobacteria Dep., Div. Diagnostics, Statens Serum Institut, Artillerivej 5, DK-2300 Copenhagen S, Denmark

SO Infection and Immunity, (1995) Vol. 63, No. 12, pp. 4613-4618.

CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 12 Jan 1996

Last Updated on STN: 12 Jan 1996

AB The gene encoding the immunogenic protein MPT64 found in culture filtrates of Mycobacterium **tuberculosis** H37Rv was expressed in Escherichia coli K-12 and purified as a recombinant protein. The purified recombinant MPT64 elicited delayed-type hypersensitivity (DTH) in outbred guinea pigs sensitized with Mycobacterium bovis BCG Tokyo. The skin reactions were comparable to those obtained with native MPT64. No skin reactions were observed when either recombinant MPT64 or native MPT64 was used in guinea pigs sensitized with M. bovis BCG Danish 1331. Amino- and carboxy-terminal deletion mutants of MPT64 were purified as fusion proteins for the mapping of DTH-inducing epitopes on recombinant MPT64 by use of the guinea pig skin test model. The part of the molecule responsible for the biological activity was located at the carboxy-terminal end. Further studies with overlapping synthetic peptides have pinpointed the biological activity at a single DTH-inducing epitope consisting of 15 residues between amino acids Gly-173 and Ala-187. Screening by PCR of 56 clinical isolates of M. **tuberculosis** from Danish and Tanzanian patients demonstrated the presence of mpt64 in all of the strains. These results point to MPT64 as a possible candidate for a skin test reagent specific for diagnosis of human **tuberculosis**.

L11 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on  
STN DUPLICATE 9

AN 1994:271662 BIOSIS

DN PREV199497284662

TI Cloning and B-cell-epitope mapping of MPT64 from Mycobacterium **tuberculosis** H37Rv.

AU **Oettinger, Thomas** [Reprint author]; Andersen, Ase B.

CS Mycobacteria Dep., Sector Biotechnol., Statens Serum Institut, Artillerivej

5, DK-2300 Copenhagen S, Denmark  
 SO Infection and Immunity, (1994) Vol. 62, No. 5, pp. 2058-2064.  
 CODEN: INFIBR. ISSN: 0019-9567.  
 DT Article  
 LA English  
 OS EMBL-X75361  
 ED Entered STN: 24 Jun 1994  
 Last Updated on STN: 24 Jun 1994  
 AB The gene of the immunogenic protein MPT64 found in culture filtrates of Mycobacterium **tuberculosis** H37Rv was cloned and sequenced. A comparison showed mpt64 and the gene encoding MPB64 from Mycobacterium bovis BCG Tokyo to be identical except for one silent mutation. The regions encoding the promoter and the signal peptide were also well conserved for the two sequences. Southern blot experiments on genomic mycobacterial DNA showed the presence of mpt64 in the M. **tuberculosis** substrains H37Rv, H37Ra, and Erdman and in the M. bovis BCG substrains Tokyo, Moreau, and Russian, whereas the M. bovis BCG substrains Glaxo, Pasteur, Canadian, Tice, and Danish 1331 and Mycobacterium leprae lack the gene. Southern blot analyses revealed differences in the restriction enzyme patterns within the M. **tuberculosis** substrains as well as within the M. bovis BCG substrains, indicating either different chromosomal localization of mpt64 or that mutations have occurred at different locations on the chromosomes. N-terminal and C-terminal deletion mutants were constructed for the mapping of B-cell epitopes on MPT64 with five monoclonal antibodies, C24b1, C24b2, C24b3, L24b4, and L24b5. Western blot (immunoblot) analysis revealed that the murine antibodies bind to one linear and three conformational epitopes.

=> s tuberculosis and (RD1-ORF5)

L12 14 TUBERCULOSIS AND (RD1-ORF5)

=> dup rem l12

PROCESSING COMPLETED FOR L12

L13 10 DUP REM L12 (4 DUPLICATES REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L13 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1

AN 2004:490265 CAPLUS

DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. **tuberculosis**, and use thereof as vaccines and in diagnosis

IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

PA Den.

SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		

DK 1998-1281                    A            19981008  
EP 1998-913536                A3          19980401

- AB The present invention is based on the identification and characterization of a number of **M. tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.
- TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis
- AB The present invention is based on the identification and characterization of a number of **M. tuberculosis** derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.
- ST sequence Mycobacterium culture filtrate antigen gene; **tuberculosis** vaccine diagnosis Mycobacterium culture filtrate antigen gene
- IT 213992-10-0P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**M. tuberculosis** culture filtrate antigen CFP29 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)
- IT 706035-97-4P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**M. tuberculosis** culture filtrate antigen CFP30A N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)
- IT 213992-24-6P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**M. tuberculosis** culture filtrate antigen CFP30B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)
- IT 213992-20-2P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**M. tuberculosis** culture filtrate antigen CFP50 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)
- IT 213992-21-3P  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**M. tuberculosis** culture filtrate antigen CFP7B N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)
- IT 213992-11-1P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(M. **tuberculosis** culture filtrate antigen CFPSA N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-89-4P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(M. **tuberculosis** culture filtrate antigen CFPSB N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 213992-13-3P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(M. **tuberculosis** culture filtrate antigen CWP32 N-terminal peptide; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-88-3P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-23-6 706035-25-8 706035-27-0 706035-29-2 706035-31-6  
706035-33-8 706035-35-0 706035-37-2 706035-39-4 706035-41-8  
706035-43-0 706035-45-2 706035-47-4 706035-49-6 706035-51-0  
706035-53-2 706035-55-4 706035-57-6 706035-59-8 706035-61-2  
706035-63-4 706035-65-6 706035-67-8 706035-69-0 706035-71-4  
706035-73-6 706035-75-8 706035-77-0 706035-79-2 706035-81-6  
706035-83-8 706035-85-0

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-87-2

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-22-5 706035-24-7 706035-26-9 706035-28-1 706035-30-5  
706035-32-7 706035-34-9 706035-36-1 706035-38-3 706035-40-7  
706035-42-9 706035-44-1 706035-46-3 706035-48-5 706035-50-9  
706035-52-1 706035-54-3 706035-56-5 706035-58-7 706035-60-1  
706035-62-3 706035-64-5 706035-66-7 706035-68-9 706035-70-3  
706035-72-5 706035-74-7 706035-76-9 706035-78-1 706035-80-5  
706035-82-7 706035-84-9

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706035-86-1

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M.

**tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-03-5 706036-04-6 706036-05-7 706036-06-8 706036-07-9  
706036-08-0 706036-09-1 706036-10-4 706036-11-5 706036-12-6

706036-13-7	706036-14-8	706036-15-9	706036-16-0	706036-17-1
706036-18-2	706036-19-3	706036-20-6	706036-21-7	706036-22-8
706036-23-9	706036-24-0	706036-25-1	706036-26-2	706036-27-3
706036-28-4	706036-29-5	706036-30-8	706036-31-9	706036-32-0
706036-33-1	706036-34-2	706036-35-3	706036-36-4	706036-37-5
706036-38-6	706036-39-7	706036-40-0	706036-41-1	706036-42-2
706036-43-3	706036-44-4	706036-45-5	706036-46-6	706036-47-7
706036-48-8	706036-49-9	706036-50-2	706036-51-3	706036-52-4
706036-53-5	706036-54-6	706036-55-7	706036-58-0	706036-59-1
706036-60-4	706036-61-5	706036-62-6	706036-63-7	706036-64-8
706036-65-9	706036-66-0	706036-67-1	706036-68-2	706036-69-3
706036-70-6	706036-71-7	706036-72-8	706036-73-9	706036-74-0
706036-75-1	706036-76-2	706036-77-3	706036-78-4	706036-79-5

RL: PRP (Properties)

(unclaimed nucleotide sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as vaccines and in diagnosis)

IT 706036-56-8 706036-57-9 706036-80-8 706036-81-9

RL: PRP (Properties)

(unclaimed protein sequence; cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to **M. tuberculosis**, and use thereof as v

# SYSTEM LIMITS

EXCEEDED

L13 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

AN 2004:59568 CAPLUS

DN 140:127185

TI Antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment

IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas

PA Den.

SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		

DK 1993-798	A	19930702
US 1993-123182	B2	19930920
WO 1994-DK273	A2	19940701
US 1995-465640	A1	19950605
DK 1997-376	A	19970402
US 1997-44624P	P	19970418
EP 1998-913536	A3	19980401
US 1999-289388	B2	19990412

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1-ORF5**, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

TI Antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and **RD1-ORF5**, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

ST *Mycobacterium* antigen vaccine **tuberculosis** diagnosis

IT Antigens

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**RD1-ORF5**; antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2653c; antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2654c; antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT *Mycobacterium bovis*

(antigen **RD1-ORF5** expressed in; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antigens in; antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Animal

Human

(diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT **Tuberculosis**

(diagnosis, **tuberculosis**; antigens from *Mycobacterium* as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
(immunodiagnosis; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Drug delivery systems  
(injections, intradermally; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins  
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)  
(monoclonal; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Epitopes  
Molecular cloning  
Mycobacterium **tuberculosis**  
**Tuberculosis**  
Tuberculostatics  
Vaccines  
(protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Immunoassay  
(skin test; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
(**tuberculosis, tuberculosis**; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT Immunization  
(vaccination; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium  
(virulent; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Interferons  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\gamma$ ; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 649655-13-0 649655-14-1 649655-15-2 649655-16-3 649655-17-4  
649655-18-5 649655-19-6 649655-20-9  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT 649655-09-4 649655-10-7 649655-11-8 649655-12-9  
RL: PRP (Properties)  
(unclaimed protein sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

IT 649543-98-6 649544-02-5 649544-05-8 649544-08-1 649544-11-6  
649544-14-9 649544-18-3 649544-21-8 649544-24-1 649544-27-4  
649544-30-9 649544-33-2 649544-36-5 649544-40-1 649544-43-4  
649544-46-7 649544-49-0 649544-52-5 649544-55-8 649544-58-1  
649544-61-6 649544-65-0 649544-68-3 649544-71-8 649544-74-1  
649544-79-6 649544-82-1 649544-85-4 649544-88-7 649544-91-2  
649544-94-5 649544-97-8 649545-00-6 649545-03-9 649545-06-2  
649545-09-5 649545-12-0 649545-15-3 649545-18-6 649545-21-1  
649545-24-4 649545-27-7 649545-30-2 649545-33-5 649545-36-8  
649545-39-1 649545-42-6 649545-45-9 649545-48-2 649545-51-7  
649545-54-0 649545-57-3 649655-21-0 649655-22-1 649655-23-2  
649655-24-3 649655-25-4 649655-26-5 649655-27-6 649655-28-7  
649655-29-8 649655-30-1  
RL: PRP (Properties)  
(unclaimed sequence; antigens from Mycobacterium as vaccine and uses in **tuberculosis** diagnosis and treatment)

L13 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:60336 CAPLUS

DN 140:144681

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

IN Andersen, Peter; Rosenkrands, Ida; Stryhn, Anette  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 76 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006952	A2	20040122	WO 2003-DK477	20030708
	WO 2004006952	A3	20040318		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1523331	A2	20050420	EP 2003-763613	20030708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2004057963	A1	20040325	US 2003-617038	20030711
PRAI	DK 2002-1098	A	20020713		
	US 2002-401725P	P	20020807		
	WO 2003-DK477	W	20030708		

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**

AB The present invention is based on a number of M. **tuberculosis** derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

ST Mycobacterium **tuberculosis** low oxygen induced antigen gene vaccine diagnostic

; BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(γ; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT	650674-04-7P	650674-05-8P	650674-06-9P	650674-07-0P	650674-08-1P
	650674-09-2P	650674-10-5P	650674-11-6P	650674-12-7P	650674-13-8P
	650674-14-9P	650674-15-0P	650674-16-1P	650674-17-2P	650674-18-3P
	650674-19-4P	650674-20-7P	650674-21-8P	650674-22-9P	650674-23-0P
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	650674-39-8P	650674-40-1P	650674-41-2P	650674-42-3P	650674-43-4P
	650674-44-5P	650674-45-6P	650674-46-7P	650674-47-8P	650674-48-9P
	651361-06-7P				

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of **tuberculosis**)

IT 7782-44-7, Oxygen, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(low; Mycobacterium low oxygen-induced antigens and genes for vaccines

or diagnostics of **tuberculosis**)

IT	650674-49-0P	650674-50-3P	650674-51-4P	650674-52-5P	650674-53-6P
	650674-54-7P	650674-55-8P	650674-56-9P	650674-57-0P	650674-58-1P
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	650674-64-9P	650674-65-0P	650674-66-1P	650674-67-2P	650674-68-3P
	650674-69-4P	650674-70-7P	650674-71-8P	650674-72-9P	650674-73-0P
	650674-74-1P	650674-75-2P	650674-76-3P	650674-77-4P	650674-78-5P
	650674-79-6P	650674-80-9P	650674-81-0P	650674-82-1P	650674-83-2P
	650674-84-3P	650674-85-4P	650674-86-5P	650674-87-6P	650674-88-7P
	650674-89-8P	650674-90-1P	650674-91-2P	650674-92-3P	650674-93-4P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);  
DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)

(nucleotide sequence; Mycobacterium low oxygen-induced antigens and  
genes for vaccines or diagnostics of **tuberculosis**)

IT	650674-94-5	650674-95-6	650674-96-7	650674-97-8	650674-98-9
	650674-99-0	650675-00-6	650675-01-7	650675-02-8	650675-03-9
	650675-04-0	650675-05-1	650675-06-2	650675-07-3	650675-08-4
	650675-09-5	650675-10-8	650675-11-9	650675-12-0	650675-13-1
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	650675-34-6	650675-35-7	650675-36-8	650675-37-9	650675-38-0
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	650675-44-8	650675-45-9	650675-46-0	650675-47-1	650675-48-2
	650675-49-3	650675-50-6	650675-51-7	650675-52-8	650675-53-9
	650675-54-0	650675-55-1	650675-56-2	650675-57-3	650675-58-4
	650675-59-5	650675-60-8	650675-61-9	650675-62-0	650675-63-1
	650675-64-2	650675-65-3	650675-66-4	650675-67-5	650675-68-6
	650675-69-7	650675-70-0	650675-71-1	650675-72-2	650675-73-3
	650675-74-4	650675-75-5	650675-76-6	650675-77-7	650675-78-8
	650675-79-9	650675-80-2	650675-81-3	650675-82-4	650675-83-5
	650675-84-6	650675-85-7			

RL: PRP (Properties)

(unclaimed sequence; mycobacterium low oxygen-induced antigens and  
genes for vaccines or diagnostics o

SYSTEM LIMITS EXCEEDED

L13 ANSWER 4 OF 10 USPATFULL on STN

AN 2004:76186 USPATFULL

TI Therapeutic TB vaccine

IN Andersen, Peter, Bronshoj, DENMARK  
Rosenkrands, Ida, Vaerloose, DENMARK  
Stryhn, Anette, Virum, DENMARK

PI US 2004057963 A1 20040325

AI US 2003-617038 A1 20030711 (10)

PRAI DK 2002-1098 20020713  
US 2002-401725P 20020807 (60)

DT Utility

FS APPLICATION

LREP HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321  
NORRISTOWN ROAD, SPRING HOUSE, PA, 19477

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

DRWN 7 Drawing Page(s)

LN.CNT 6018

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Therapeutic vaccines comprising polypeptides expressed during the latent  
stage of mycobacteria infection are provided, as are multiphase  
vaccines, and methods for treating and preventing **tuberculosis**

AB . . . expressed during the latent stage of mycobacteria infection are  
provided, as are multiphase vaccines, and methods for treating and  
preventing **tuberculosis**.

SUMM [0002] The present invention discloses a therapeutic vaccine against  
latent or active **tuberculosis** infection caused by the

**tuberculosis** complex microorganisms (Mycobacterium **tuberculosis**, M.bovis, M.africanum). The invention furthermore discloses a multi-phase vaccine that can be administered either prophylactically or therapeutically as well as a diagnostic reagent for the detection of latent stages of **tuberculosis**.

SUMM [0003] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent decades this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM [0004] Organisms of the **tuberculosis** complex can cause a variety of diseases, but the commonest route of invasion is by inhalation of bacteria. This initiates. . . for the rest of their life. Certainly, individuals who have been healthy for years or even decades can suddenly develop **tuberculosis**, which has proven to be caused by the same organism they were infected with many years previously. M. **tuberculosis** and other organisms of the TB complex are unique in that the mycobacteria can evade the immune response and survive.

SUMM [0005] The course of a M. **tuberculosis** infection runs essentially through 3 phases, as illustrated in FIG. 1. During the acute phase, the bacteria proliferate in the. . . a latent phase is established where the bacterial load is kept stable at a low level. In this phase M. **tuberculosis** goes from active multiplication to dormancy, essentially becoming non-replicating and remaining inside the granuloma. In some cases, the infection goes. . .

SUMM [0009] It has been suggested that the transition of M. **tuberculosis** from primary infection to latency is accompanied by changes in gene expression (see, for example, Honer zu Bentrup, 2001, which.

SUMM . . . candidate. The only way to determine if a protein is recognized by the immune system during latent infection with M. **tuberculosis** is to produce the given protein and test it in an appropriate assay as described herein. Of the more than.

DRWD . . . the infection. For analysis of therapeutic vaccinations a reactivation model is established, where aerosol infected mice are treated with anti-M **tuberculosis** drugs for 8 weeks from the peak of infection (6 weeks after infection). This induces a latent infection phase with.

DRWD . . . In FIG. 2A, the immunization was given as a prophylactic vaccine 6 weeks before the mice were given a M. **tuberculosis** infection (approx. 250 bacilli) through the aerosol route with. Bacterial numbers in the lung was enumerated 6 weeks post infection..

DETD [0024] The invention is related to preventing, treating and detecting infections caused by species of the **tuberculosis** complex (Mycobacterium **tuberculosis**, M. bovis, M. africanum) by the use of a polypeptide comprising a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof, or by the use of a DNA sequence encoding a M. **tuberculosis** antigen or an immunogenic portion or other variant thereof. The invention discloses a new therapeutic vaccine against **tuberculosis** comprising antigens induced during the latent stage of TB-infection. It also discloses a multiphase vaccine incorporating a combination of prophylactic and therapeutic antigens as well as diagnostic reagents for the detection of the latent stage of M. **tuberculosis** infection.

DETD . . . mycobacteria infection, which stage is characterized by low-oxygen tension in the microenvironment of the mycobacteria, for a therapeutic vaccine against **tuberculosis**.

DETD . . . with efficacy as prophylactic vaccines, where the fusion partner is selected from e.g. the group consisting of ESAT-6, TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

DETD [0033] The invention further discloses a therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments

hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection, . . .

DETD [0036] The invention also discloses a method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the above-mentioned vaccine.

DETD [0037] The invention also discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the above mentioned vaccine.

DETD . . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being.

DETD . . . use of a nucleic acid fragment according to the invention for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, and the use of a nucleic acid fragment according to the invention for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g., by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

DETD . . . a still further embodiment, the invention discloses a vaccine for immunizing an human being or other mammal or animal, against **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a . . .

DETD [0049] (b) isolating the polypeptide from a whole mycobacterium, e.g. *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, from culture filtrate or from lysates or fractions thereof; or

DETD [0051] The invention also discloses a method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . immunogenic composition as defined above, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis**

DETD [0052] In another embodiment, the invention discloses a method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the polypeptide as defined above, the immunogenic composition according to.

DETD . . . detecting binding of a antibody to said polypeptide, said binding being an indication that said subject is infected by *Mycobacterium tuberculosis* or is susceptible to *Mycobacterium tuberculosis* infection.

DETD [0082] A preferred polypeptide within the present invention is an immunogenic antigen from *M. tuberculosis* produced when the organism is subjected to the stresses associated with latent infection. Such antigen can for example also be derived from the *M. tuberculosis* cell and/or *M. tuberculosis* culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native *M. tuberculosis* antigen or be heterologous and such sequences may, but need not, be immunogenic.

DETD . . . any other antigen with which it is natively associated, i.e.

free of any other antigen from bacteria belonging to the **tuberculosis** complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in.

DETD [0085] By the term "virulent mycobacterium" is understood a bacterium capable of causing the **tuberculosis** disease in an animal or in a human being. Examples of virulent mycobacteria include but are not limited to *M. tuberculosis*, *M. africanum*, and *M. bovis*.

DETD Examples of relevant animals are cattle, possums, badgers and kangaroos. [0088] By "a latently infected individual" is understood an individual, who has been infected by a virulent mycobacterium, e.g. *M. tuberculosis*, but shows no sign of active **tuberculosis**.

. It is likely that individuals who have been vaccinated, e.g. by BCG, or treated for TB may still retain the. . . for PPD reactivity. Nonetheless, in its most accurate sense, "latently-infected" may be used to describe any individual who has *M. tuberculosis* residing in their tissues but who is not clinically ill.

DETD [0101] In the context of providing candidate molecules for a new vaccine against **tuberculosis**, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been shown (Olsen, 2000) that.

DETD . . . response may also be determined by the use of T cell lines derived from an immune individual or an *M. tuberculosis* -infected person where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture.

DETD [0114] In general, *M. tuberculosis* antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures.

DETD [0115] They may be purified as native proteins from the *M. tuberculosis* cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a.

DETD . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from *M. tuberculosis*, such as of a polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystalline, or at least one T-cell.

DETD . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other *M. tuberculosis* antigens and/or a carrier, vehicle and/or adjuvant substance.

DETD . . . from *M. leprae*. Antigens with therapeutic properties may be identified based on their ability to diminish the severity of *M. tuberculosis* infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic.

DETD [0161] Cloning and Expression of Low Oxygen Induced *M. tuberculosis* Antigens in *E. coli*.

DETD [0162] A number of *M. tuberculosis* genes are induced under low oxygen conditions. The upregulation of the genes listed in table 2 has been determined at.

DETD . . . Ammonium Sulfate, 0.2 mM of each of the four nucleotides, 0.2  $\mu$ M of each primer and 10 ng of *M. tuberculosis* H37Rv chromosomal DNA. The reaction mixtures were initially heated to 95° C. for 5 min., followed by 35 cycles of:

DETD . . . with recombinant antigens. Six weeks after the last immunization, the mice are given an aerosol infection with approximately 250 *M. tuberculosis* bacilli. The protective capacity of the vaccine is evaluated by enumeration of the bacteria in spleen and lung 6 weeks.

DETD . . . reactivation model of latent TB has been established (van Pinxteren, 2000) (FIG. 1B). An aerosol infection with approximately 250 *M. tuberculosis* bacilli is given and at the peak of infection 6 weeks later, the mice receive an 8-week course of anti-mycobacterial.

DETD . . . cells is significantly higher in the unimmunized group. ESAT6

is an antigen produced in high amounts by the actively-growing M. **tuberculosis** bacteria. The level of the ESAT6 specific immune response in infected mice could therefore be indicative the degree of actively-growing. . . have in fact demonstrated such a correlation between the level of ESAT6 response and degree of disease in both M. **tuberculosis**-infected humans and M. bovis-infected cattle (Doherty, 2002, Vordermeier, 2002). Therefore, the higher ESAT6 response in the unimmunized group of latently-infected.

DETD . . . lungs of the Rv0569 vaccinated mice, whereas neither ESAT6 nor BCG are able to inhibit the growth of the M. **tuberculosis** bacteria when given as a vaccine during latent infection. That is, the induction of Rv0569 T cell responses can participate. . .

DETD [0182] Anon. 2001. Global **Tuberculosis** Control. WHO Report.

DETD [0202] Danish Patent application PA 2000 00666 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0203] Danish Patent application PA 1999 01020 (WO 01/23388) " **Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD [0204] Patent application U.S. Ser. No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis** "

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 273

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

Val Glu Pro Lys Arg Ser Arg Leu Val Val Cys Ala Pro Glu Pro Ser

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 152

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 2

Met Ser Pro Gly Ser Arg Arg Ala Ser Pro Gln Ser Ala Arg Glu Val

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 3

LENGTH: 114

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 3

Val Glu Ser Glu Pro Leu Tyr Lys Leu Lys Ala Glu Phe Phe Lys Thr

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 4

LENGTH: 344

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 4

Met Pro Ile Ala Thr Pro Glu Val Tyr Ala Glu Met Leu Gly Gln Ala

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 5

LENGTH: 113

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 5

Met Gly Glu His Ala Ile Lys Arg His Met Arg Gln Arg Lys Pro Thr

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 6

LENGTH: 380

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 6

Val Ala Gly Asn Pro Asp Val Val Thr Val Leu Leu Gly Gly Asp Val

1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 7  
LENGTH: 397  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 7  
Val Thr Asp His Val Arg Glu Ala Asp Asp Ala Asn Ile Asp Asp Leu  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 8  
LENGTH: 446  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 8  
Met Val Glu Pro Gly Asn Leu Ala Gly Ala Thr Gly Ala Glu Trp Ile  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 9  
LENGTH: 210  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 9  
Met Ile Ala Thr Thr Arg Asp Arg Glu Gly Ala Thr Met Ile Thr Phe  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 10  
LENGTH: 80  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 10  
Met Thr Asn Val Gly Asp Gln Gly Val Asp Ala Val Phe Gly Val Ile  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 11  
LENGTH: 652  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 11  
Val Thr Val Thr Pro Arg Thr Gly Ser Arg Ile Glu Glu Leu Leu Ala  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 12  
LENGTH: 395  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 12  
Met Arg Gly Gln Ala Ala Asn Leu Val Leu Ala Thr Trp Ile Ser Val  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 13  
LENGTH: 94  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 13  
Met Cys Gly Asp Gln Ser Asp His Val Leu Gln His Trp Thr Val Asp  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 14  
LENGTH: 560  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 14  
Met Ile Pro Thr Met Thr Ser Ala Gly Trp Ala Pro Gly Val Val Gln  
1                    5                    10. . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 15  
LENGTH: 143

TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 15  
 Met Ile Thr Asn Leu Arg Arg Arg Thr Ala Met Ala Ala Ala Gly Leu  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 16  
 LENGTH: 905  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 16  
 Leu Ser Ala Ser Val Ser Ala Thr Thr Ala His His Gly Leu Pro Ala  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 17  
 LENGTH: 258  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 17  
 Met Ser Phe His Asp Leu His His Gln Gly Val Pro Phe Val Leu Pro  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 18  
 LENGTH: 285  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 18  
 Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 19  
 LENGTH: 285  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 19  
 Val Val Lys Arg Ser Arg Ala Thr Arg Leu Ser Pro Ser Ile Trp Ser  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 20  
 LENGTH: 114  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 20  
 Val Thr Tyr Val Ile Gly Ser Glu Cys Val Asp Val Met Asp Lys Ser  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 21  
 LENGTH: 279  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 21  
 Met Asn Gln Ser His Lys Pro Pro Ser Ile Val Val Gly Ile Asp Gly  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 22  
 LENGTH: 339  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 22  
 Met Thr Glu Pro Ala Ala Trp Asp Glu Gly Lys Pro Arg Ile Ile Thr  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 23  
 LENGTH: 681  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 23  
 Val Leu Met Thr Ala Ala Ala Asp Val Thr Arg Arg Ser Pro Arg Arg

1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 24  
LENGTH: 144  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 24  
Met Ala Thr Thr Leu Pro Val Gln Arg His Pro Arg Ser Leu Phe Pro  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 25  
LENGTH: 331  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 25  
Met Pro Asp Thr Met Val Thr Thr Asp Val Ile Lys Ser Ala Val Gln  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 26  
LENGTH: 195  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 26  
Met Pro Leu Leu Thr Ile Gly Asp Gln Phe Pro Ala Tyr Gln Leu Thr  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 27  
LENGTH: 272  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 27  
Met Ser Gly Arg Gly Glu Pro Thr Met Lys Thr Ile Ile Val Gly Ile  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 28  
LENGTH: 393  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 28  
Met Arg Asp Ala Ile Pro Leu Gly Arg Ile Ala Gly Phe Val Val Asn  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 29  
LENGTH: 413  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 29  
Met Ala Ser Ser Ala Ser Asp Gly Thr His Glu Arg Ser Ala Phe Arg  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 30  
LENGTH: 120  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 30  
Met Ser Thr Gln Arg Pro Arg His Ser Gly Ile Arg Ala Val Gly Pro  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 31  
LENGTH: 374  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 31  
Met Arg Ser Glu Arg Leu Arg Trp Leu Val Ala Ala Glu Gly Pro Phe  
1                    5                    10. . . .  
DETD    SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 32  
LENGTH: 179

TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 32  
 Met Leu His Arg Asp Asp His Ile Asn Pro Pro Arg Pro Arg Gly Leu  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 33  
 LENGTH: 375  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 33  
 Val Thr Gln Thr Gly Lys Arg Gln Arg Arg Lys Phe Gly Arg Ile Arg  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 34  
 LENGTH: 371  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 34  
 Met Arg Val Gly Ile Pro Thr Glu Thr Lys Asn Asn Glu Phe Arg Val  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 35  
 LENGTH: 104  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 35  
 Met Val Ile Arg Phe Asp Gln Ile Gly Ser Leu Val Leu Ser Met Lys  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 36  
 LENGTH: 344  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 36  
 Val Leu Lys Asn Ala Val Leu Leu Ala Cys Arg Ala Pro Ser Val His  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 37  
 LENGTH: 336  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 37  
 Val Trp Ser Ala Ser Gly Gly Gln Cys Gly Lys Tyr Leu Ala Ala Ser  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 38  
 LENGTH: 110  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 38  
 Val Val Gln Gly Arg Thr Val Leu Phe Arg Thr Ala Glu Gly Ala Lys  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 39  
 LENGTH: 463  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 39  
 Met Asn His Leu Thr Thr Leu Asp Ala Gly Phe Leu Lys Ala Glu Asp  
 1 5 10.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 40  
 LENGTH: 332  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 40  
 Met Asn Thr His Phe Pro Asp Ala Glu Thr Val Arg Thr Val Leu Thr

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 41

LENGTH: 578

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 41

Met Thr Thr Gly Gly Leu Val Asp Glu Asn Asp Gly Ala Ala Met Arg

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 42

LENGTH: 268

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 42

Met Ser Asp Pro Arg Pro Ala Arg Ala Val Val Val Gly Ile Asp Gly

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 43

LENGTH: 181

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 43

Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 44

LENGTH: 274

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 44

Met Thr Trp Ala Asp Glu Val Leu Ala Gly His Pro Phe Val Val Ala

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 45

LENGTH: 248

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 45

Val Ser Asp Gly Glu Gln Ala Lys Ser Arg Arg Arg Arg Gly Arg Arg

1 5 10. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 46

LENGTH: 819

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 46

gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60

ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120

gctcgtgccg tgggtcgcggt gttggccgat cggggcgta ccgggggtgc. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 47

LENGTH: 819

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 47

gtggaaccga aacgcagtcg cctcgtcgta tgtgcacccg agccatcgca cgcgcgggaa 60

ttcccggatg tcgccgtatt ctccggcggc cgggctaacg catcccaggc cgaacggttg 120

gctcgtgccg tgggtcgcggt gttggccgat cggggcgta ccgggggtgc. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 48

LENGTH: 342

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 48

gtggagtcg aaccgctgta caagctcaag gcggagttct tcaaaaccct tgcgcatccg 60

gcgcggatca ggattttgga gctgctggtc gagcgggacc gttcggtcgg tgagttgctg 120

tcctcggacg tcggcctgga gtcgtcgaac ctgtcccagc agctgggtgt. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 49

LENGTH: 1032

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 49

atgcctatcg caacgcccga ggtctacgcg gagatgctcg gtcaggccaa acaaaaactcg	60
tacgctttcc cggctatcaa ctgcacctcc tcggaaaccg tcaacgccgc gatcaaagg	120
ttcgccgacg ccggcagtga cggaatcatc cagttctcga ccggtggcgc.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 50

LENGTH: 339

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 50

atgggtgagc acgccatcaa gcggcacatg cggcaacgga agcctacgaa gcatccccta	60
gcccagaaac ggggcgcgcg gattctggtc ttcaccgacg atccccgcag gagcgtcctc	120
atagtgcgcc gttgccacct ggattccatg cgccgagaaa agaacycgt.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 51

LENGTH: 1140

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 51

gtggctggca atcctgatgt ggtgacggcg ctgctgggcg gtgacgtcat gtcgggccgt	60
ggcgctgatc agatcctgcc tcatcccggc aaaccgcaat tgcgcgaacg gtatatgcgg	120
gatgcgaccg gctatgttcg cctggccgag cgggtgaacg ggcgcattcc.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 52

LENGTH: 1191

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 52

gtgacagacc acgtgcgcga ggcggacgac gcgaacatcg acgatctgtt gggcgacctg	60
ggcgggtaccg cgcgcgccga gcgtgcgaag cttgtcgagt gggtgctcga gcagggcatc	120
acccccgacg agattcgggc gaccaaccgc ccgttgctgc tggccaccgc.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 53

LENGTH: 1338

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 53

atggtagagc ccggcaattt ggcaggcgcg accggcgccg aatggatcgg ccggccaccg	60
cacgaggaat tgcagcgcaa agtgcgcccg ctgctgccat ccgacgatcc gttctacttc	120
ccacctgccc gctaccagca tgccgtgccc ggaacgggtg tgcgctcgcg.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 54

LENGTH: 630

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 54

atgatcgcca caaccgcga tcgtgaagga gccaccatga tcacgtttag gctgcgcttg	60
ccgtgccgga cgatactgcg ggtgttcagc cgcaatccgc tgggtcgtgg gacggatcga	120
ctcgaggcgg tcgtcatgct gctggccgtc acggtctcgc tgctgactat.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 55

LENGTH: 240

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 55

atgaccaacg tcggtgacca ggggggttgac gcggtcttcg ggggtgatcta cccacctcag	60
gtcgcgctgg tcagtttcgg caagccggca caacgagttt gcgccgtcga cggcgcgatc	120
cacgtcatga cgaccgtgct ggctacgctg cccgctgacc acggctgcag.	

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 56

LENGTH: 1956

TYPE: DNA

ORGANISM: *Mycobacterium tuberculosis*

SEQUENCE: 56  
 gtgacgggtga caccacggac cggcagccgc atcgaggagc tgcttgacac cagcggcccg 60  
 ttcttcatcc cgggtgagat ctccggcgat ctgcgtaccg tgaccgcccg cggcggcccg 120  
 gacggcgacg tgttctatcg agaccgggtg agccacgaca aggtggtccg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 57  
 LENGTH: 1185  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 57  
 atgagagggc aagcggccaa tctcgtgctg gccacctgga tctcgggtgt caacttctgg 60  
 gcgtggaacc tgatcggccc gctgtcgacc agctacgcgc gtgacatgtc actgtccagc 120  
 gccgaggcgt cgctgctcgt cgccaccccg atcctggtgg gtgcccttgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 58  
 LENGTH: 282  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 58  
 atgtgcggcg accagtccga tcacgtgctg cagcactgga ccgtcgacat atcgatcgac 60  
 gaacacgaag gattgactcg ggcgaaggca cggctgcgtt ggcgggaaaa ggaattggtg 120  
 ggtgttgcc tggcaaggct caatccggcc gaccgcaacg tccccgagat.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 59  
 LENGTH: 1680  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 59  
 atgattccca cgatgacatc ggccggctgg gcaccagggg tgggtgcagtt ccgcgaatac 60  
 caacggcggt ggctgcgcgg cgatgtcctc gccggcctga ccgtggccgc ctatctgac 120  
 ccgcaagcga tggcgatgc gaccgtggcg ggcctaccgc cggcagccgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 60  
 LENGTH: 429  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 60  
 atgatacaaa acctccgacg ccgaaccgcg atggcagccg ccggcctagg ggctgctctc 60  
 gggctgggca tctgctggt tccgacggtg gacgcccac tcgccaacgg ttcgatgtcg 120  
 gaagtcata tgctggaaat tgccgggttg cctatccctc cgattatcca.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 61  
 LENGTH: 2715  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 61  
 ttgtcggcgt cagtgtctgc cagcagcgt catcatggct tgccagcaca tgaagtgggtg 60  
 ctgctgctgg agagcgatcc atatcacggg ctgtccgacg gcgaggccgc ccaacgacta 120  
 gaacgcttcg ggccaacac cttggcggtg gtaacgcgcg ctagcttgct.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 62  
 LENGTH: 774  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 62  
 atgagtttcc acgatcttca tcaccaaggt gttccgttcg tgttgcccaa cgcttgggat 60  
 gtgccgtcgg ccctggccta cctcgcggag ggcttcacgg ctatcggcac aaccagtttc 120  
 ggggtctcgt ccagcggcgg gcacccggac gggcaccgcg ccactcgcgg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 63  
 LENGTH: 855  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 63  
 gtgggtcaagc gctctcgggc aaccggactt tcgccgagca tctgggtccgg atgggaatca 60  
 cctcagtgtc ggtccattcg ggcgcgattg ctgctacccc ggggtcggtc gcggccggcg 120  
 aacgccgatt gttgctggaa tcagctcgcg gtgacgcctg acaccgggat.  
 DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 64  
 LENGTH: 885  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 64  
 atgtctaaac cccgaagca gcacggagtt gtcgtcgggg tagatgggtc gctcgaatcg 60  
 gatgccgccc cctgttgggg tgccaccgat gcggcgatga ggaacattcc gctgaccgtg 120  
 gtccacgtgg tgaacgccga ttagcgacg tggccgccga tgccgtatcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 65  
 LENGTH: 342  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 65  
 gtgacctatg tgatcggtag tgagtgcgtg gatgtgatgg acaagtcctg tgtgcaggag 60  
 tgtccggtcg actgtatcta tgagggcgcc cgaatgctct acatcaaccc cgacgagtgc 120  
 gtggattgtg gtgcgtgcaa accggcctgc cgcgtcgagg cgatctactg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 66  
 LENGTH: 837  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 66  
 atgaaccaat cacacaaacc cccatcgatc gtcgtcggta ttgatggctc gaagccggcc 60  
 gtgcaagccg cactgtgggg ggtcgacgag gcagccagcc gtgacatccc gctgcgtctg 120  
 ctgtacgca tcgaacccga cgatcccggg tacgccgcac acggcgcgcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 67  
 LENGTH: 1017  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 67  
 atgacggagc cagcggcgtg ggacgaaggc aagccgcgaa tcatcacttt gaccatgaac 60  
 cccgccttgg acatcacgac gagcgtcgac gtgggtgcgg ccgaccgagaa aatgcgttgt 120  
 ggcgcacctc gctacgatcc cggcggcgcc ggtatcaatg tcgcccgcac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 68  
 LENGTH: 2043  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 68  
 gtgctgatga ccgcagcggc tgatgtcacc cggcgctcgc cgcggcgcggt gttccgtgac 60  
 cgccgcgagg ccggccgggt gctggcgga ttactcgccg cctatcgga ccagccggac 120  
 gtgattgtgc tcggcttggc ccgggggtgg ctcccggtcg catgggaggt. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 69  
 LENGTH: 432  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 69  
 atggccacca cccttcccgt tcagcgccac ccgcgggtccc tcttccccga gttttctgag 60  
 ctgttcgcgg ccttcccgtc attcgccgga ctccggccca ccttcgacac ccggttgatg 120  
 cggctggaag acgagatgaa agagggggcg tacgaggtac gcgcggagct. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 70  
 LENGTH: 993  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 70  
 atgccggaca ccatggtgac caccgatgtc atcaagagcg cgggtgcagtt ggcctgccgc 60  
 gcaccgtcgc tccacaacag ccagccctgg cgctggatag ccgaggacca cacggttgcg 120  
 ctgttcctcg acaaggatcg ggtgctttac gcgaccgacc actccggccg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 71  
 LENGTH: 585  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 71

atgccactgc taaccattgg cgatcaattc cccgcctacc agtcaccgc tctcatcggc 60  
 ggtgacctgt ccaaggtcga cgccaagcag cccggcgact acttcaccac tatcaccagt 120  
 gacgaacacc caggcaagtg gcgggtggtg ttcttttggc cgaaagactt. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 72  
 LENGTH: 816  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 72  
 atgtctggga gaggagagcc gacgatgaaa acaatcattg ttggtatcga tggttcgcac 60  
 gcggcgatta cggccgcatt gtgggggggtt gacgaggcca tcagccgagc ggtgccgctg 120  
 cgactggtct cagtgatcaa gccgacacat ccgtccccgg acgactacga. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 73  
 LENGTH: 1179  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 73  
 atgcgtgatg cgatccccgt tgggcggatc gccgggtttg tggatgaacgt ccactggagc 60  
 gtgttggtga tcctgtgggt gttcacctgg agtctggcga ccatgttgcc gggtagcgtc 120  
 ggaggctacc cggccgtggt ctattggctt ctcggcgtag gtggcgcggt. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 74  
 LENGTH: 1239  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 74  
 atggcaagtt ctgcgagcga cggcaccac gaacgctcgg cttttcgctt gaggccaccg 60  
 gtcttgagcg gcgccatggg accgttcatt cacaccgggc tgtacgtcgc tcaatcgtgg 120  
 cgcgactatc tgggtcaaca gcccataaaa ctgccgatcg cacggccac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 75  
 LENGTH: 360  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 75  
 atgtccacgc aacgaccgag gcactccggt attcgggctg ttggccccta cgcattgggccc 60  
 ggccgatgtg gtcggatagg caggtggggg gtgcaccagg aggcgatgat gaatctagcg 120  
 atatggcacc cgcgcaaggt gcaatccgcc accatctatc aggtgaccga. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 76  
 LENGTH: 1122  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 76  
 atgcgatcag aacgtctccg gtggctggta gccgcagaag gtccgttcgc ctcggtgtat 60  
 ttcgacgact cgcacgacac tcttgatgcc gtcgagcgcc ggggaagcgac gtggcgcgat 120  
 gtccggaagc atctcgaaag ccgcgacgcy aagcaggagc tcacgacag. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 77  
 LENGTH: 537  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 77  
 atgctgcacc gcgacgatca catcaatccg ccgcggcccc gcgggttgga tgttccttgc 60  
 gcccgcctac gagcgacaaa tcccctgcgc gccttggcgc gttgcgttca ggcgggcaag 120  
 ccgggcacca gttcagggca tcggtccgtg ccgcatacgg cggacttgcg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 78  
 LENGTH: 1125  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 78  
 gtgacgcaaa ccggcaagcg tcagagacgc aaattcggtc gcatccgaca gttcaactcc 60  
 ggccgctggc aagccagcta caccggcccc gacggccgcy tgtacatcgc ccccaaaacc 120  
 ttcaacgcca agatcgacgc cgaagcatgg ctcaccgacc gccggccgca. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 79

LENGTH: 1113  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 79  
 atgcgcgtcg gtattccgac cgagaccaa aacaacgaat tccgggtggc catcaccgcc 60  
 gccggcgtcg cggaactaac ccgtcgtggc catgaggtgc tcatccaggc aggtgccgga 120  
 gagggtcgg ctatcaccga cgcggatttc aaggcggcag gcgcgcaact. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 80  
 LENGTH: 312  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 80  
 atgggtcatcc ggtttgatca aataggggtca ttggctcctt caatgaaatc ctttgcggtca 60  
 ctgtcgtttc agcgggtgtc gcgcgagaat tctagtttgg tcgcggcgct ggaccgggtc 120  
 gatgtgcgg tcgatgagct gagecgtttg tcgtttgatg cgttgaccac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 81  
 LENGTH: 1032  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 81  
 gtgctcaaga acgcagtctt gctggcatgc cgggcgccgt cgggtgcacaa cagccagccc 60  
 tggcggtggg tggccgaaag cggctccgag cacactactg tgcacctgtt cgtcaaccgc 120  
 caccgaacgg tgccggccac cgaccattcc ggccggcaag cgatcatcag. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 82  
 LENGTH: 1011  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 82  
 gtgtgggtccg cctcgggtgg gcagtgcggg aagtatcttg ccgcctcgat ggtgctgcag 60  
 cttgatgggt tggaaagtca cgggtgtgtg gagtttgggc gtgaccgcta tggccccgag 120  
 gtgcgtgagg agctgttggc gatgagtgcg gccagcatcg atcgttatct. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 83  
 LENGTH: 330  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 83  
 gtgggtgcaag gccgcaccgt gctgtttcgt accgcggagg gcgccaaatt attttcagcc 60  
 gtcgcgaagt gcgcgggtggc ttctgaggcg gacgaccaca acgttgccga gggctggagc 120  
 gtgatcgtca aggttcgcgc ccagggtgctg acgaccgacg cgggggtccg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 84  
 LENGTH: 1389  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 84  
 atgaatcacc taacgacact tgacgccggg tttctcaagg cagaagacgt ggatcggcac 60  
 gtgagtctgg caatcggcgc tctggcggtc atcgaggggc cggctcccga tcaggaagcc 120  
 ttcttatcgt cgctcgtca acgcctacgt ccctgtaccc ggttcgggca. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 85  
 LENGTH: 996  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 85  
 atgaacaccc atttcccgga cgccgaaacc gtgcgaacgg ttctcaccct ggccgtccgg 60  
 gccccctcca tccacaacac gcagccggtg cgggtggcggg tatgcccagc gagtctggag 120  
 ctgttctcta gacccgatat gcagctgcgt agcaccgatc cggacgggcg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 86  
 LENGTH: 1734  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 86  
 atgacaacag ggggcctcgt cgacgaaaac gacggcgccg caatgcgtcc actgcgtcac 60

acgctctccc aactacgcct gcacgagctg ctggctcgagg tgcaggaccg ggtcgagcag 120  
atcgctcgagg gccgggaccg cctcgatggg ctgggtggagg ccatgctcgt. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 87

LENGTH: 804

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 87

atgagcgcgt ctcggccagc tcgggcagtg gtcgttggtg tgcacgggtc aagggcggca 60  
acgcatgcgg cgttgtgggc ggtcgatgag gcggtgaacc gagacattcc gctgcgactg 120  
gtgtacgtca tcgatccgtc ccaactgtcc gccgccggcg agggcgggtg. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 88

LENGTH: 543

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 88

atgacagaat acgaagggcc taagacaaaa ttccacgcgt taatgcagga acagattcat 60  
aacgaattca cagcggcaca acaatatgtc gcgatcgagg tttatttcga cagcgaagac 120  
ctgccgcagt tggcgaagca tttttacagc caagcggtcg aggaacgaaa. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 89

LENGTH: 822

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 89

atgacatggg ccgacgaggt gctcgccgga catccctttg tggttgctca ccgtgggtgcg 60  
tcggcggtc gcggcgagca tacccttgcc gcctacgacc tggcgctcaa agagggcgcc 120  
gacggcggtg aatgtgatgt gcgggttgacc cgggacgggc atctggtctg. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 90

LENGTH: 744

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 90

gtgtccgacg gcgaacaagc caaatcacgt cgacgccggg ggccggcgccg cgggcggcgcc 60  
gctgcggcta cagccgagaa tcacatggac gcccaaccgg ccggcgacgc caccgccgacc 120  
ccggcaacgg cgaagcggtc ccgggtccgc tcacctcgtc gcgggtcgac. . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 91

LENGTH: 88

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 91

Met Lys Ala Lys Val Gly Asp Trp Leu Val Ile Lys Gly Ala Thr Ile

1 5 10. . .

CLM What is claimed is:

1. A method for inducing an immune response to latent **tuberculosis** in an individual, said method comprising the step of delivering a composition comprising one or more polypeptides or fragments thereof, . . .
2. The method according to claim 1, wherein said individual is infected by a virulent mycobacterium, e.g. M. **tuberculosis**, and is not vaccinated with BCG against **tuberculosis**.

6. A therapeutic vaccine against **tuberculosis** comprising one or more polypeptides or fragments hereof, which polypeptides are expressed during the latent stage of the mycobacteria infection, . . .  
vaccine according to claim 9 where the fusion partners is selected from the group consisting of ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein, MPT32.

13. A multiphase vaccine according to claim 12 where the antigen components with prophylactic activity comprises ESAT-6, ESAT-6-Ag85B, TB10.4, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, Ag85B (MPT59), MPB59, Ag85C, 19 kDa lipoprotein or MPT32.

18. A method for treating an animal, including a human being, with **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the vaccine according to claim 6.

19. A method for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, comprising administering to the animal the vaccine according to claim 12.

20. A method of diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being, comprising application or intradermally injecting, in the animal, . . . encoding these polypeptides, a positive skin response at the location of injection or application being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection or application being indicative of the animal not having **tuberculosis**.

22. A method of diagnosing *Mycobacterium tuberculosis* infection in a subject comprising: (a) contacting a polypeptides or fragments hereof, which polypeptides are expressed during the latent stage. . . detecting binding of an antibody to said polypeptide, said binding being an indication that said subject is infected by *Mycobacterium tuberculosis* or is susceptible to *Mycobacterium tuberculosis* infection.

L13 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk

PA Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. comps. such as diagnostic reagents containing

the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing **tuberculosis** caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating **tuberculosis** using antigens isolated from *Mycobacterium tuberculosis*.

ST *Mycobacterium* antigen sequence **tuberculosis** diagnosis treatment

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(Ag85A, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(Ag85B, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(Ag85C, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(CFP10, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(ESAT-6, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(MPB59, in fusion protein; protein and DNA sequences of antigens from *Mycobacterium* and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(MPB64, in fusion protein; protein and DNA sequences of antigens from

Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(MPT32, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(MPT64, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(RD1-ORF2, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(RD1-ORF5, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv0652/CFP16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(Rv1036, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv1636/TB15A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv1984c/CFP21; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Rv2185c/TB16; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study,

unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Rv2462c/TB51; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Rv2623/TB32; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Rv3354/CFP8A; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Rv3451/CFP23; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Rv3872/RD1-ORF3; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Antigens  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (TB10.4, in fusion protein; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Diagnosis  
 (agents, **tuberculosis**; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cell membrane  
 Cell wall  
 (antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Fusion proteins (chimeric proteins)  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (antigens in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Cytoplasm  
 (cytosol, antigen isolated from; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Animal  
 Human  
 (diagnosis of **tuberculosis** in; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT Mycobacterium avium  
 Mycobacterium intracellulare  
 Mycobacterium marinum

Mycobacterium scrofulaceum  
 Mycobacterium szulgai  
 Mycobacterium xenopi  
 (expression of antigen CFP21 and CFP23 in; protein and DNA sequences of  
 antigens from Mycobacterium and uses in **tuberculosis**  
 diagnosis and treatment)

IT Mycobacterium fortuitum  
 Mycobacterium kansasii  
 (expression of antigen CFP23 in; protein and DNA sequences of antigens  
 from Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Diagnosis  
 (immunodiagnosis; protein and DNA sequences of antigens from  
 Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Lipoproteins  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic  
 use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological  
 study); USES (Uses)  
 (in fusion protein; protein and DNA sequences of antigens from  
 Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Antibodies and Immunoglobulins  
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (monoclonal; protein and DNA sequences of antigens from Mycobacterium  
 and uses in **tuberculosis** diagnosis and treatment)

IT DNA sequences  
 Epitopes  
 Immunoassay  
 Molecular cloning  
 Mycobacterium **tuberculosis**  
 Protein sequences  
**Tuberculosis**  
 Tuberculostatics  
 (protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment)

IT Antibodies and Immunoglobulins  
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP  
 (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (protein and DNA sequences of antigens from Mycobacterium and uses in  
**tuberculosis** diagnosis and treatment)

IT Diagnosis  
 (serodiagnosis; protein and DNA sequences of antigens from  
 Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT Mycobacterium africanum  
 Mycobacterium bovis  
 Mycobacterium **tuberculosis**  
 (**tuberculosis** caused by; protein and DNA sequences of  
 antigens from Mycobacterium and uses in **tuberculosis**  
 diagnosis and treatment)

IT Mycobacterium  
 (virulent; protein and DNA sequences of antigens from Mycobacterium and  
 uses in **tuberculosis** diagnosis and treatment)

IT Crystallins  
 RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic  
 use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological  
 study); USES (Uses)  
 ( $\alpha$ -, in fusion protein; protein and DNA sequences of antigens  
 from Mycobacterium and uses in **tuberculosis** diagnosis and  
 treatment)

IT 592558-08-2P 592558-09-3P 592558-10-6P 592558-11-7P 592558-12-8P

592558-13-9P 592558-14-0P 592558-15-1P 592558-16-2P, Antigen T51

(Mycobacterium **tuberculosis**)

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592557-99-8 592558-00-4 592558-01-5 592558-02-6 592558-03-7  
592558-04-8 592558-05-9 592558-06-0 592558-07-1

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-15-4 592573-16-5 592573-17-6 592573-18-7 592573-19-8  
592573-20-1 592573-21-2 592573-22-3 592573-23-4 592573-24-5  
592573-26-7 592573-27-8 592573-28-9 592573-29-0 592573-30-3  
592573-31-4 592573-32-5 592573-33-6

RL: PRP (Properties)

(unclaimed nucleotide sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 592573-14-3 592573-25-6

RL: PRP (Properties)

(unclaimed protein sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

IT 213992-11-1 213992-15-5 264285-55-4 264285-57-6 264285-59-8

RL: PRP (Properties)

(unclaimed sequence; protein and DNA sequences of antigens from Mycobacterium and uses in **tuberculosis** diagnosis and treatment)

L13 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

AN 2003:609858 CAPLUS

DN 139:163576

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

IN Andersen, Peter; Skjot, Rikke Louise Vinther

PA Den.

SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
	W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA			
	RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	EP 1508339	A1	20050223	EP 2004-77505	19940701
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI			
	US 5955077	A	19990921	US 1995-465640	19950605
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY			
	US 2004013685	A1	20040122	US 2001-872505	20010601

PRAI	DK 1993-798	A	19930702
	US 1993-123182	B2	19930920
	WO 1994-DK273	A2	19940701
	US 1995-465640	A1	19950605
	DK 1997-376	A	19970402
	US 1997-44624P	P	19970418
	DK 1997-1277	A	19971110
	US 1998-70488P	P	19980105
	US 1999-289388	B2	19990412
	EP 1994-919574	A3	19940701
	EP 1998-913536	A3	19980401
	US 1998-246191	B2	19981230
	DK 1999-1020	A	19990713
	US 1999-144011P	P	19990715
	US 2000-615947	A2	20000713
	WO 2000-DK398	A2	20000713
	US 2001-804980	A2	20010313

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

TI Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex

AB The present invention is based on the identification and characterization of a number of novel M. **tuberculosis** derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, **RD1-ORF5**, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

ST Mycobacterium **tuberculosis** antigen gene antibody vaccine diagnosis skin test

; DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT	575512-14-0	575512-20-8	575512-21-9	575512-22-0	575512-23-1
	575512-24-2	575512-25-3	575512-26-4	575512-27-5	575512-28-6
	575512-29-7	575512-30-0	575512-31-1	575512-32-2	575512-33-3
	575512-34-4	575512-35-5	575512-36-6	575512-37-7	575512-38-8
	575512-39-9	575512-40-2	575512-41-3	575512-43-5	575512-45-7
	575512-47-9	575512-49-1	575512-51-5	575512-53-7	575512-55-9
	575512-57-1	575512-59-3	575512-66-2	575512-67-3	575512-68-4
	575512-69-5	575512-70-8	575512-71-9	575512-72-0	575512-73-1
	575512-74-2	575512-75-3	575512-76-4	575512-77-5	575512-78-6
	575512-79-7	575512-80-0	575512-81-1	575512-82-2	575512-83-3
	575512-84-4	575512-85-5	575512-86-6	575512-87-7	575512-88-8
	575512-89-9	575512-90-2	575512-91-3	575512-92-4	575512-93-5
	575512-94-6	575512-95-7	575512-96-8	575512-97-9	575513-00-7
	575513-01-8	575513-02-9	575513-03-0	575513-04-1	575513-05-2
	575513-06-3	575513-07-4	575513-08-5	575513-10-9	575513-12-1
	575513-14-3	575513-15-4	575513-16-5	575513-17-6	575513-18-7
	575513-19-8	575513-20-1	575513-21-2	575513-22-3	575513-23-4
	575513-24-5	575513-25-6	575513-26-7	575513-27-8	575513-32-5
	575513-34-7	575513-36-9	575513-37-0	575513-39-2	575513-40-5
	575513-41-6	575513-42-7	575513-43-8	575513-44-9	575513-45-0

RL: PRP (Properties)

(unclaimed nucleotide sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused

by species of the **tuberculosis** complex)

IT	575512-15-1	575512-16-2	575512-17-3	575512-18-4	575512-19-5
	575512-42-4	575512-44-6	575512-46-8	575512-48-0	575512-50-4
	575512-52-6	575512-54-8	575512-56-0	575512-58-2	575512-60-6
	575512-61-7	575512-62-8	575512-63-9	575512-64-0	575512-65-1
	575512-98-0	575512-99-1	575513-09-6	575513-11-0	575513-13-2
	575513-29-0	575513-30-3	575513-31-4	575513-33-6	575513-35-8
	575513-38-1				

RL: PRP (Properties)

(unclaimed protein sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

IT	213992-07-5	213992-08-6	213992-10-0	213992-11-1	213992-13-3
	213992-14-4	213992-15-5	213992-16-6	213992-17-7	213992-18-8
	213992-19-9	213992-20-2	213992-21-3	213992-23-5	213992-24-6

RL: PRP (Properties)

(unclaimed sequence; mycobacterium **tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the **tuberculosis** complex)

# SYSTEM LIMITS EXCEEDED

L13 ANSWER 7 OF 10 USPATFULL on STN

AN 2003:291011 USPATFULL

TI Nucleic acids fragments and polypeptide fragments derived from M. **tuberculosis**

IN Andersen, Peter, Br.o slashed.nsh.o slashed.j, DENMARK  
 Nielsen, Rikke, Frederiksberg, DENMARK  
 Oettinger, Thomas, Hellerup, DENMARK  
 Rasmussen, Peter Birk, K.o slashed.benhaven, DENMARK  
 Rosenkrands, Ida, K.o slashed.benhaven, DENMARK  
 Weldingh, Karin, K.o slashed.benhaven, DENMARK  
 Florio, Walter, Frederiksberg, DENMARK

PA Statens Serum Institut, Copenhagen, DENMARK (non-U.S. corporation)

PI US 6641814 B1 20031104

AI US 1998-50739 19980330 (9)

PRAI DK 1997-376 19970402

US 1997-44624P 19970418 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Swartz, Rodney P

LREP Frommer Lawrence & Haug, Kowalski, Thomas J.

CLMN Number of Claims: 43

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 5870

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

TI Nucleic acids fragments and polypeptide fragments derived from M. **tuberculosis**

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, . . .)

SUMM The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the Mycobacterium **tuberculosis**, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of

production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from *M. tuberculosis* which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with *M. tuberculosis*. The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.

SUMM Human *tuberculosis* (hereinafter designated "TB") caused by *Mycobacterium tuberculosis* is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of *M. tuberculosis*.

SUMM Immunity to *M. tuberculosis* is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations;. . . molecule seems to be interferon gamma (INF- $\gamma$ ). Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from *M. tuberculosis* during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested.

SUMM . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from *M. tuberculosis*. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21 respectively), shows homology to two *M. tuberculosis* DNA sequences, orf19A and orf23. The two sequences, orf19a and orf23, encode to putative proteins CFP19A and CFP23 with the.

SUMM The present invention is also based on the identification of a number of putative antigens from *M. tuberculosis* which are not present in *Mycobacterium bovis* BCG strains. The nucleotide sequences encoding these putative antigens are:

SUMM rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b.

SUMM . . . 152 153

RD1-ORF8 67 68

RD1-ORF2 71 72

RD1-ORF9B 69 70

RD1-ORF3 87 88

RD1-ORF9A 93 94

RD1-ORF4 89 90

**RD1-ORF5** 91 92

MPT59- 172

ESAT6

ESAT6- 173

MPT59

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the *tuberculosis* complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the *tuberculosis* complex, or

SUMM . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the *tuberculosis* complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the *tuberculosis* complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the *tuberculosis* complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell.

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the *M. tuberculosis* derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48,. . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections

with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by *Mycobacterium bovis* BCG and also at least. . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of *M. tuberculosis*, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance.

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g.. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals.

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which.

SUMM The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium bovis* BCG, and *Mycobacterium africanum*.

SUMM . . . other short peptide sequences), whereas the product which can be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and.

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenged infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml, . . .

SUMM 3) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the *M. tuberculosis* protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a *M. tuberculosis* protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first. . .

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a *M. tuberculosis* polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the *M.*

**tuberculosis** proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin).

SUMM isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. *M. smegmatis*, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extra-cellular antigens, or because of their absence in *M. bovis* BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other *M. tuberculosis* antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the *M. tuberculosis* complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act.

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as.

SUMM The invention also relates to a method of diagnosing TB caused by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis* in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide.

SUMM . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described.

SUMM . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that *M. tuberculosis*, e.g. *esat-6* is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as *M. . .* . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have.

SUMM . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the.

DRWD FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with *M. tuberculosis*. Mice were given a challenge of *M. tuberculosis* and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of.

DRWD . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with *M. tuberculosis* and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN- $\gamma$  was investigated

DRWD . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in *M. tuberculosis*

H37Rv.

DETD A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10.sup.4 M.

**tuberculosis** i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were.

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 M. **tuberculosis** i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly.

DETD The recombinant  $\lambda$ gt11 M. **tuberculosis** DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB.

DETD In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb M. **tuberculosis** derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+ (Stratagene) and used to transform E. coli.

DETD Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb M. **tuberculosis** derived EcoRI-EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+ (Stratagene) and used to transform E. coli.

DETD . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the M. **tuberculosis** genome was performed in the Sanger database (Sanger Mycobacterium **tuberculosis** database):

DETD . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and M. **tuberculosis** and M. bovis has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new M. **tuberculosis** specific diagnostic antigens as well as antigens for a new vaccine against TB, the RD1 region (17.499 bp) of M. **tuberculosis** H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted.

DETD Identification of the ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b.

DETD The nucleotide sequence of rdl-orf2 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of rdl-orf3 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of rdl-orf4 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of **rdl-orf5** from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of rdl-orf8 from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of rdl-orf9a from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD The nucleotide sequence of rdl-orf9b from M. **tuberculosis** H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD Cloning of the ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b

DETD The ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b were PCR cloned in the pMST24 (Theisen et al., 1995) (rdl-orf3) or the pQE32 (QIAGEN) (rdl-orf2, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b) expression vector. Preparation of oligonucleotides and PCR amplification of the rdl-orf encoding genes, was carried out as described in example 2. Chromosomal DNA from M. **tuberculosis** H37Rv was used as

template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from.

DETD **rd1-orf5**. A BamHI site was engineered immediately 5' of the first codon of **rd1-orf5**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rd1-orf5** was subcloned in pQE32, giving pTO88.

DETD Purification of Recombinant RD1-ORF2, RD1-ORF3, RD1-ORF4, **RD1-ORF5**, RD1-ORF8, RD1-ORF9a and RD1-ORF9b.

DETD The nucleotide sequences of **rd1-orf2**, **rd1-orf3**, **rd1-orf4**, **rd1-orf5**, **rd1-orf8**, **rd1-orf9a**, and **rd1-orf9b** from *M. tuberculosis* H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of **rd1-orf2**, **rd1-orf3**, **rd1-orf4**, **rd1-orf5**, **rd1-orf8**, **rd1-orf9a**, and **rd1-orf9b** are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 35 94, and 70,.

DETD the Linocin M18 protein from *Brevibacterium linens*, a set of degenerated primers were constructed for PCR cloning of the *M. tuberculosis* gene encoding CFP29. PCR reactions were containing 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 µM of each of the four nucleotides (Boehringer Mannheim),.

DETD first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD (<http://www.sanger.ac.uk/projects/M-tuberculosis/blast.sub.13> server).

DETD This program identified a Mycobacterium **tuberculosis** sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29.

DETD sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in *M. tuberculosis* culture filtrate is 175 amino acids. This gives a theoretical molecular weight at 18517 Da and a pI at 6.8..

DETD PCR reactions contained 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),.

DETD sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD were found in the Sanger database. This could be due to the fact that only approximately 70% of the *M. tuberculosis* genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining.

DETD CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two Mycobacterium **tuberculosis** sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second,.

DETD CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative *M. tuberculosis* thymidylate synthase (450 aa accession No p28176).

DETD PCR reactions contained 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),.

DETD sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** genome database:

DETD <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD PCR reactions contained 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),.

DETD were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from *M. tuberculosis*

H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994)...

DETD The nucleotide sequence of the cloned 952 bp M. **tuberculosis** H37Rv PCR fragment, pTO52, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . . .

DETD . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. **tuberculosis** H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version where amino acids 1-15 have been deleted. The deletion includes. . . .

DETD PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+low salt Taq+buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer Mannheim),. . . .

DETD

#### TABLE 5

IFN- $\gamma$  release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. **tuberculosis** after stimulation with

native antigens.

Antigen.sup.a IFN- $\gamma$  (pg/ml).sup.b

ST-CF 12564

CFP7 .sup. ND.sup.d

CFP9 ND

CFP17 9251

CFP20 2388

CFP21 10732

DETD The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . . .

DETD

#### TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**, after stimulation with native antigens.

Antigen.sup.a Skin reaction (mm).sup.b

Control 2.00

PPD.sup.c 15.40 (0.53)

CFP7 ND.sup.e

CFP9 ND

CFP17 11.25. . . .

DETD

#### TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10.sup.4 CFU of M. **Tuberculosis**.

Antigen.sup.a Skin reaction (mm).sup.b

Control 2.9 (0.3)

PPD.sup.c 14.5 (1.0)

CFP 7a 13.6 (1.4)

CFP 17 6.8 (1.9)

CFP 20. . . .

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were. . . .

DETD . . . female C57BL/6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

DETD . . . +++ +  
rCFP29 +++ +++ +++ ++  
rMPT51 + - - -

Mouse IFN- $\gamma$  release during recall of memory immunity to M. **tuberculosis**.

-: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.

DETD . . . rCFP21 +++  
rCFP22 -  
rCFP29 +  
rCFP25 +++  
rMPT51 +

Mouse IFN- $\gamma$  release 14 days after primary infection with M. **tuberculosis**.

-: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.

DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD 6 weeks after the last immunization the mice were aerosol challenged with 5+10.sup.6 viable Mycobacterium **tuberculosis**/ml. After 6 weeks of infection the mice were killed and the number of viable bacteria in lung and spleen of.

DETD Species Distribution of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b as well as of cfp7a, cfp7b, cfp10a, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a

DETD Presence of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b in Different Mycobacterial Species

DETD In order to determine the distribution of the cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes in species belonging to the M. **tuberculosis**-complex and in other mycobacteria PCR and/or Southern blotting was used. The bacterial strains used are listed in TABLE 10. Genomic.

DETD . . . were used in order to determine the distribution of the cfp7, cfp9 and mpt51 gene in species belonging to the **tuberculosis**-complex and in other mycobacteria. The bacterial strains used are listed in TABLE 10. PCR was performed on genomic DNA prepared.

DETD  
TABLE 10

Mycobacterial strains used in this Example.  
Species and strain(s) Source

1. M. **tuberculosis** H37R v

ATCC.sup.a  
(ATCC  
27294)

2. H37R

aATCC  
(ATCC  
25177)

3. Erdman Obtained from A. Lazlo,  
Ottawa, Canada

4. . . .

DETD . . . United Kingdom) with a vacuum transfer device (Milliblot, TM-v; Millipore Corp., Bedford, Mass.). The cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b gene fragments were amplified by PCR from the plasmids pRVN01, pRVN02, pTO52, pTO87, pTO88, pTO89, pTO90, . . .

DETD cfp7, cfp9 and mpt51 were found in the M. tuberculosis complex including BCG and the environmental mycobacteria; M. avium, M. kansasii, M. marinum M. intracellular and M. flavescens. cfp9 was.

DETD There is a strong band at around 26 kDa in M. tuberculosis H37Rv, Ra, Erdman, M. bovis AN5, M. bovis BCG substrain Danish 1331 and M. africanum. No band was seen in.

DETD  
TABLE 13a

Interspecies analysis of the rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b genes by Southern blotting.  
Species and strain rdl-orf2 rdl-orf3 rdl-orf4 **rdl-orf5** rdl-orf8 rdl-orf9a rdl-orf9b

- 1. M. tub. H37Rv + + + + + + +
- 2. M. bovis + + + + N.D.. . .

DETD Positive results for rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b were only obtained when using genomic DNA from M. tuberculosis and M. bovis, and not from M. bovis BCG or other mycobacteria analyzed except rdl-orf4 which also was found in.

DETD Southern blotting was carried out as described for rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b, The cfp7a, cfp7b, cfp10a, cfp17, cfp20, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a gene fragments were.

DETD  
GENERAL INFORMATION:  
NUMBER OF SEQ ID NOS: 173  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 1  
LENGTH: 381  
TYPE: DNA

ORGANISM: Mycobacterium tuberculosis  
SEQUENCE: 1  
ggccgcccgt acctatgtgg ccgccgatgc tgcggacgcg tcgacctata ccgggttctg 60  
atcgaaacct gctgaccgag aggacttgtg atgtcgcaaa tcatgtacaa ctaccccgcg 120  
atgttgggtc acgccgggga tatggccgga tatgccgga cgctgcagag cttgggtgcc 180  
gagatcgccg tggagcaggc. . . gccatggaag atttgggtgc ggcctatcat 300  
gcgatgtcca gcacccatga agccaacacc atggcgatga tggcccgcga caccgcccga 360  
gccgccaaat ggggcggcta g 381

SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 2  
LENGTH: 96  
TYPE: PRT  
ORGANISM: Mycobacterium tuberculosis  
SEQUENCE: 2  
Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly  
1 5 10 15  
Asp. . . Asp Thr Ala Glu Ala Ala Lys Trp Gly Gly  
85 90 95

SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 3  
LENGTH: 467  
TYPE: DNA  
ORGANISM: Mycobacterium tuberculosis  
SEQUENCE: 3  
gggtagccgg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg 60  
gcgacggcgt cataaaccgg gacggcacct tggtggcggg ccccgcggtg ctgacgcccg 120  
acgagtacaa ctcccggctg gtggccgccc acccggaagtc caccgcggcg ttgcccgcag 180  
gcgcccggct ggtcgttctg. . . cgacccatc 360  
gcgacctcat tgccggagaa atcttggcta ccgacttcga attcgccgac ctcgccgatg 420  
gtgtggccat cggcgacggc gtgcgggtaa gcatcgaaaa gacctga 467

SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 4  
LENGTH: 108  
TYPE: PRT  
ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 4  
Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly  
1 5 10 15  
Leu. . . Gly Asp Gly Val Arg Val Ser Ile Glu Lys Thr  
100 105

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 5

LENGTH: 889

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 5

cgggtctgca	cggatccggg	cgggacaggg	caatcgagcc	tgggatccgc	tggggtgctg	60
acatcgcgga	cccgtgcgcg	gtacggtcga	gacagcggca	cgagaaagta	gtaagggcga	120
taataggcgg	taaagagtag	cgggaagccg	gccgaacgac	tcggtcagac	aacgccacag	180
cggccagtga	ggagcagcgg.	. . .	ccatctccaa	780		
gattcgattc	ttggaggctg	agggctctgt	gacgccccgg	cgggcctcat	cggggtatcg	840
gcggttcacc	gcatacgact	gcgcacggct	gcgattcatt	ctcactgcc		889

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 6

LENGTH: 162

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 6

Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu	
1 5 10 15	
Val. . . Gln Gly Glu Asp Asp Gly Ser Thr Gly	
145 150 155 160	

Gly Pro

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 7

LENGTH: 898

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 7

tcgactccgg	cgccaccggg	caggatcacg	gtgtcgacgg	ggtcgcccgg	gaatcccacg	60
ataaccactc	ttcgcccat	gaatgccagt	gttggccagg	cgctggcctg	gcgtccacgc	120
cacacaccgc	acagattagg	acacgccggc	ggcgcagccc	tgcccgaag	accgtgcacc	180
ggtcttgga	gactgtgccc.	. . .	780			
ggcggtaata	caggtgcagg	tcgtgctccc	acgtgaaggc	gatggcaccg	tggatctgaa	840
gagcggagcc	ggcgcataac	acaaagggtt	ccgcggctctg	cgccttcgcc	agcggcgc	898

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 8

LENGTH: 165

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 8

Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu	
1 5 10 15	
Leu. . . Tyr Glu Ala Ala Leu	
145 150 155 160	

Ala Ala Leu Gly Ala

165

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 9

LENGTH: 1054

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 9

ataatcagct	caccgttggg	accgacctcg	accaggggtc	ctttgtgact	gccgggcttg	60
acgcggacga	ccacagagtc	ggatcatgcc	taaggctacc	gttctgacct	ggggctgcgt	120
gggcggccgac	gacgtgaggc	acgtcatgtc	tcagcggccc	accgccacct	cggtcgcccgg	180
cagtatgtca	gcatgtgcag.	. . .	gccggatgaa	atgacggtcg	960	
ggcggtaatc	gtttgtgttg	aacgcgtaga	gccgatcacc	gccggggctg	gtgtagacct	1020
caatgtttgt	gttcgccggc	agggttccgg	atcc			1054

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 10

LENGTH: 217

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 10

Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr

1 5 10 15

Thr. . . 195 200 205

Ala Ala Asn Arg Leu Asp His Ala Gly

210 215

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 11

LENGTH: 949

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 11

agccgctcgc gtgggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60

gtccggggcgc aggcttgccg tcaataactc ggtcaagttc cttcacagac tgccatcact 120

ggcccgctcgc cgggctcgtt gcgggtgcgc cgcgtgcggg tttgtgttcc gggcaccggg 180

tgggggccc cccgggcgta. . . ggccgttcaa 840

ccggacgccc tcacgccaag tccgctcacc tttggccgcg accggcgtaa ccggcagcgg 900

taagcgcac gagcacctcc actgggtcgc tgccgagatc ccagcggga 949

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 12

LENGTH: 182

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 12

Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr

1 5 10 15

Ala. . . Pro Val Val Ile

165 170 175

Glu Ser Ile Thr Ile Ser

180

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 13

LENGTH: 1060

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 13

tggaccttca ccggcgggtcc cttcgtttcg ggggcgcacac ctaacatact ggtcgtcaac 60

ctaccgcgac accgctggga ctttgtgcca ttgccggcca ctccggggccg ctgcggcctg 120

gaaaaattgg tcgggcacgg gcggccgcgg gtcgctacca tccactgtg aatgatttac 180

tgacccgcgc actgctcacc. . . tatcaagaca agaagggagt 960

aggcgtatgca cgcaaaagtc ggcgactacc tcgtggtgaa gggcacaacc acggaacggc 1020

atgatcaaca tgctgagatc atcgaggtgc gctccgcaga 1060

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 14

LENGTH: 219

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 14

Met Gly Ala Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro

1 5 10 15

Ile. . . 205

Gln Ala Ala Asp Phe Val Ala Gly Lys Leu Gln

210 215

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 15

LENGTH: 1198

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 15

cagatgctgc gcaacatgtt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60

ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120

ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgct atcgatcggc 180

agcttgaaaag gaagcccccg. . . 1080

ggcctggaag acgggtgcggg ctaggcggcg tttgaggcag cgtagtgctg cgcgtttggt 1140

tttcccggcg tcttgagacc tttggtagta ggcctggccc cggctgtcgg tcatccgg 1198

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 16

LENGTH: 265  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 16  
Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp  
1 5 10 15  
Ala. . . 245 250 255  
Ala Glu Ala Ser Val Ala Leu Ser His  
260 265

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 17

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: VARIANT

LOCATION: (1)

OTHER INFORMATION: Ala is Ala or Ser

SEQUENCE: 17

Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr Glu Xaa Ala Val  
1 5 10 15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 18

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 18

Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu  
1 5 10 15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 19

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (3)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 19

Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly Thr His  
1 5 10 15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 20

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 20

Thr Asn Ser Pro Leu Ala Thr Ala Thr Leu His Thr Asn  
1 5 10 15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 21

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (2)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 21

Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg Phe Glu  
1 5 10 15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 22

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (1)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 22  
 Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala Asp Glu  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 23  
 LENGTH: 19  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 23  
 Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp  
 1 5 10 15  
 Ala Glu Ile  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 24  
 LENGTH: 34  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 24  
 cccggctcga gaacctstac cgcgacctsg csc 34  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 25  
 LENGTH: 37  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 25  
 gggccggatc cgasgcsgcg tccttsacs gytgcc 37  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 26  
 LENGTH: 28  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 26  
 ggaagcccca tatgaacaat ctctaccg 28  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 27  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM:  
 DETD Mycobacterium **tuberculosis**  
 SEQUENCE: 27  
 cgcgctcagc ccttagtgac tgagcgcgac cg 32  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 28  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 28  
 ctcgaattcg ccgggtgcac acag 24  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 29  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 29  
 ctcgaattcg cccccatacg agaac 25  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 30  
 LENGTH: 15  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 30  
 gtgtatctgc tggac 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 31  
 LENGTH: 15  
 TYPE: DNA

ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 31	
ccgactggct ggccg	15
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 32	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 32	
gaggaattcg cttagcggat cgca	24
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 33	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 33	
cccacattcc gttgg	15
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 34	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 34	
gtccagcaga tacac	15
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 35	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 35	
gtacgagaat tcatgtcgca aatcatg	27
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 36	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 36	
gtacgagaat tcgagcttgg ggtgccg	27
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 37	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 37	
cgattccaag cttgtggccg ccgacccg	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 38	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 38	
cgttagggat cctcatcgcc atggtgttgg	30
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 39	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 39	
cgttagggat ccggttccac tgtgcc	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 40	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 40	
cgttagggat cctcaggtct tttcgatg	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 41	

LENGTH: 952  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 41  
 gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg 60  
 cgctgtctcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggg gtcgcggtag 120  
 ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg tcgccctcga 180  
 tgggcccggga catcccggtg. . . . 840  
 acaacggaca cttcgacttc ccagccagcg gtgacaacgg ctgggggctcg tgggcgcccc 900  
 agctgggcgc tatgtcgggc gatatcgtcg gtgcgatccg ctaagcgaat tc 952  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 42  
 LENGTH: 299  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 42  
 Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu  
 1 5 10 15  
 Ser. . . 285  
 Ala Met Ser Gly Asp Ile Val Gly Ala Ile Arg  
 290 295  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 43  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 43  
 gcaacacccg ggatgtcgca aatcatg 27  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 44  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 44  
 gtaacacccg gggtagccgc cgacccg 27  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 45  
 LENGTH: 37  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 45  
 ctactaagct tggatcccta gccgccccat ttggcgg 37  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 46  
 LENGTH: 38  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 46  
 ctactaagct tccatgggtca ggtcttttcg atgcttac 38  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 47  
 LENGTH: 450  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 47  
 gtgccgcgct ccccagggtt cttatggttc gatatacctg agtttgatgg aagtccgatg 60  
 accagcagtc agcatacggc atggccgaaa agagtggggg gatgatggcc gaggatgttc 120  
 gcgccgagat cgtggccagc gttctcgaag tcgttgtaaa cgaaggcgat cagatcgaca 180  
 agggcgacgt cgtggtgctg. . . . tcactcatgt ccacactcgg tgatctgctc 360  
 gccgaacaca cggtgctgcc gggcagcgcg gtggaccacc tgcgatcggt ggtcggggag 420  
 tggcagctcc ttgccgactt gtcgtttgcc 450  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 48  
 LENGTH: 71  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 48  
 Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val

```

1           5           10           15
Val. . . . Ala Gly

50           55           60
Asp Leu Ile Ala Val Ile Ser

65           70
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 49
LENGTH: 750
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 49
gggtacccat cgatgggttg cggttcggca ccgaggtgct aacgcacttg ctgacacact 60
gctagtgcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac 120
ttcacccgac ccgtatgccg cgctgccccaa gctgccgtcc ttcagcctga cgtcaacctc 180
gatcaccgat gggcagccgc. . . cgagcagcgt tagcgcttta gctgggttgc 660
cgacgtcttg ccgagccgac cgcttcgtgc agcgagccga acccgccgtc atgcagcctg 720
cgggcaatgc cttcatggat gtccttggcc 750
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 50
LENGTH: 176
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 50
Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser
1           5           10           15
Phe. . . . Ala Val Ile Phe Gly Thr Tyr Glu Gln Arg
165           170           175
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 51
LENGTH: 800
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 51
tcatgaggtt catcgggggtg atccccacgcc cgcagccgca ttcggggccgc tggcgagccg 60
gtgccgcacg ccgcctcacc agcctgggtg ccgccgcctt tgcggcgccg acactgttgc 120
ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag gtggtgttcg 180
cccgcggaac cggcgaacca. . . gtcgcgagca ggatctaacg cgagccgccc catagattcc 720
ggctaagcaa cggctgcgcc gccgcccggc cacgagtgc cgccgccgac tggcacaccg 780
cttaccacgg ccttatgctg 800
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 52
LENGTH: 226
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 52
Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala
1           5           10           15
Ala. . . . Asn Gln Ala Ala Arg Phe Val Ala Ser
210           215           220
Arg Ile
225
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 53
LENGTH: 700
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 53
ctaggaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt 60
aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag 120
gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc ggtttatttc 180
gacagcgaag acctgccgca. . . catcaggcgc cccgcacgct 600
gccggggggc gcctctagat ccctggcggg gatcagcgag tgggtcccgtt cgcccccccc 660
tcttcagcc aggccttggt gcggccgggg tggtagtac 700
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 54
LENGTH: 181
TYPE: PRT

```

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 54

Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln

1 5 10 15

Glu. . . Gly Ala Pro His Ala

165 170 175

Ala Gly Gly Arg Leu

180

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 55

LENGTH: 950

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 55

tgggctcggc actggctctc ccacgggtggc gcgctgattt ctccccacgg taggcgttgc 60

gacgcatgtt cttcaccgtc tatccacagc taccgacatt tgctccggct ggatcgcggg 120

taaaattccg tcgtgaacaa tcgacccatc cgctgtctga catccggcag ggctggtttg 180

ggtgcgggcg cattgatcac. . . tctgcctgga 840

tccgtcccgc agctgcccgg gtctgtcctt cagatgcccc gcactgccgc accggctccc 900

gaatcgctgc acggtcgctg acgctttgtc agtaagccca taaaatcgcg 950

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 56

LENGTH: 262

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 56

Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu

1 5 10 15

Gly. . . Ala Pro Ala Pro

245 250 255

Glu Ser Leu His Gly Arg

260

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 57

LENGTH: 1000

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 57

cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60

cttcgtccgc gcatacgtcc aaaaggcgcg acagtgacct ggccgttgcc cgatcgccctg 120

tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac tgacttctg 180

cgccgccagg cgccggagtt. . . cggagagccg gattgccgaa 900

ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 960

gagaagtga ttttccgtat ttcatctcgc ctgagcaggc 1000

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 58

LENGTH: 291

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 58

Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly

1 5 10 15

Thr. . . Asp Thr Phe Gly Ser Asp Gly

275 280 285

Gly Glu Lys

290

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 59

LENGTH: 900

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 59

ttggcccgcg cgatcatcga aagccgttcg ggtgcggata ctttcggctc cgatggcggt 60

gagaagtga ttttccgtat ttcatctcgc ctgagcaggc gatgcgcgag cgcagcgagt 120

tggcgcgtaa gggcattgcg cgggcaaaaa gcgtgggtggc gctggcctat gccggtggtg 180

tgctgttcgt cgcggagaat. . .

DETD . . . 780

gcccgcagtc tgacggcgaa tcgtcgggct gagtccgaaa gtccgacgcg tgtctgggac 840

cccgcgtgcga cgtaaactgc gcctaacccc ggctcgacgc gtcgccggcc gtcctgactt 900

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 60

LENGTH: 248

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 60

Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg

1 5 10 15

Ser. . . Ser Pro

225 230 235 240

Gln Ser Asp Gly Glu Ser Ser Gly

245

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 61

LENGTH: 1560

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 61

gagtcattgc ctggtcggcg tcattccgta ctagtccggt gtcggacttg acctactggg 60

tcaggccgac gagcactcga ccattagggg aggggccgtg acccactatg acgtcgtcgt 120

tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc tcggcctgag 180

cactgcaatc gtcgaacca. . . 1440

ggcgctgcag gagtgcttcc acggcctggt tggccacatg atcaatttct gagcgggtca 1500

tgacgaggcg cgcgagcact gacaccccc agatcatcat ggggtgccatc ggtggtgtgg 1560

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 62

LENGTH: 464

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 62

Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr

1 5 10 15

Val. . . His Gly Leu Val Gly His Met Ile Asn Phe

450 455 460

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 63

LENGTH: 550

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 63

ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60

gtagtcaccc agtaccacac accaggaagg accgcccac atggcaaagc tctccaccga 120

cgaactgctg gacgcgttca aggaaatgac cctgttgag ctctccgact tcgtcaagaa 180

gttcgaggag accttcgagg. . . gaggccgccg acgaggccaa ggccaagctg gaggccgccg

gcgccaccgt 480

caccgtcaag tagctctgcc cagcgtgttc ttttgctct gctcggccc tagcgaacac 540

tgcgccgct 550

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 64

LENGTH: 130

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 64

Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met

1 5 10 15

Thr. . . Glu Ala Ala Gly Ala Thr Val Thr

115 120 125

Val Lys

130

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 65

LENGTH: 900

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 65

tgaacgccat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60

tcttccccag gtcgtacagt cgggccatgg ccattgaggt ttcggtgttg cgggttttca 120

```

ccgattcaga cggaatttc ggtaatccgc tgggggtgat caacgccagc aaggtcgaac 180
accgcgacag gcagcagctg. . . 780
ctcagcgctg ccgatgcaac acggcggcaa ggtgatcctg caggggttgc ccgaccgcgc 840
gcattctgaa cgagtacgaa agctcgtcgc cgtcgatgcg gtaggaacgg tcaagggcgg 900
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 66
LENGTH: 228
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 66
Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly
  1           5           10           15
Asn. . . Arg Val Val Ser Asp Gly Val
  210           215           220
Ala Gln Leu Asp
225
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 67
LENGTH: 500
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 67
gtttgtggtg tcggtggtct ggggggcgcc aactgggatt cggttggggt ggggtgcaggt 60
ccggcgatgg gcattcggagg tgtgggtggg ttgggtgggg ccggttcggg tccggcgatg 120
ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat gggcatgggg 180
ggtgtgggtg gtttagatgc. . . aaacgaagca ctggggtcga agaacggctg cgctgccata 420
tcgtccggag cttccatacc ttcgtgcggc cggaagagct tgtcgtagtc ggccgcatg 480
acaacctctc agagtgcgct
500
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 68
LENGTH: 139
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 68
Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly
  1           5           10           15
Gly. . . 125
Ser Ile Pro Ser Cys Gly Arg Lys Ser Leu Ser
  130           135
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 69
LENGTH: 2050
TYPE: DNA
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 69
agcgcaactct gagaggttgt catggcggcc gactacgaca agctcttccg gccgcacgaa 60
ggtatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120
ccgccggcgc ccgcatcggc aaacctaccg aagcccaacg gccagactcc gccccgcacg 180
tccgacgacc tgtcggagcg. . . cactcgactt gtcgaccct atctacaagc gcaaggtcct
cgaattggcc 1980
gcagcgctat ccgacgattt cgagaggggt ggacgtcggt gagcgcacct gctgttgctg 2040
ctggtcctac
2050
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 70
LENGTH: 666
TYPE: PRT
ORGANISM: Mycobacterium tuberculosis
SEQUENCE: 70
Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu
  1           5           10           15
Ala. . . 650           655
Ser Asp Asp Phe Glu Arg Ala Gly Arg Arg
  660           665
SEQUENCE CHARACTERISTICS:
SEQ ID NO: 71
LENGTH: 1890
TYPE: DNA

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ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 71  
 gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgcagcga 60  
 tgaggaggag cggcgcgcat gactgctgaa ccggaagtac ggacgctgcg cgaggttggtg 120  
 ctggaccagc tcggcactgc tgaatcgct gcgtacaaga tgtggctgcc gccgttgacc 180  
 aatccggtcc cgctcaacga. . .  
 DETD . . . tcgccagacg gcaaagaggt catccaggcc 1800  
 ccctacatcg agcctccaga agaagtgttc gcagcacccc caagcgcccg ttaagattat 1860  
 ttcattgccg gtgtagcagg acccgagctc 1890  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 72  
 LENGTH: 591  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 72  
 Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp  
 1 5 10 15  
 Gln. . . Glu Val Phe Ala Ala Pro Pro Ser Ala Gly  
 580 585 590  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 73  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 73  
 Asp Pro Val Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 74  
 LENGTH: 14  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (14)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 74  
 Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly Xaa  
 1 5 10  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 75  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (5)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 75  
 Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu Ile Asp  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 76  
 LENGTH: 14  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: VARIANT  
 LOCATION: (3)  
 OTHER INFORMATION: Ala is Ala or Gln  
 SEQUENCE: 76  
 Val Ile Ala Gly Met Val Thr His Ile His Xaa Val Ala Gly  
 1 5 10  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 77  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 77  
 Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 78  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 78  
 Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 79  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 79  
 Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 80  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: VARIANT  
 LOCATION: (4)  
 OTHER INFORMATION: Asp is Asp or Glu  
 SEQUENCE: 80  
 Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala Ala Gln Leu Thr  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 81  
 LENGTH: 50  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 81  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5 10 15  
 Val. . . Val Leu Ala Glu Ala Ala Gly Thr  
 35 40 45  
 Val Ser  
 50  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 82  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 82  
 Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 83  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 83  
 Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 84  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 84  
 Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala  
 1 5 10 15  
 SEQUENCE CHARACTERISTICS:

SEQ ID NO: 85  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (10)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 85  
 Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg Glu Xaa  
     1                    5                    10                    15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 86  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 86  
 Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr  
     1                    5                    10                    15

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 87  
 LENGTH: 450  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 87  
 agcccggttaa tcgagttcgg gcaatgctga ccatcggtt tgtttccggc tataaccgaa 60  
 cggtttgtgt acgggataca aatacagga gggaagaagt aggcaaatgg aaaaaatgtc 120  
 acatgatccg atcgctgccg acattggcac gcaagtgcg gacaacgctc tgcacggcgt 180  
 gacggccggc tcgacggcgc. . . . . gggcgaagcg gtccaggacg tcgcccgcac 360  
 ctattcgcaa atcgacgacg gcgccgccgg cgtcttcgcc taataggccc ccaacacatc 420  
 ggaggggagt atcaccatgc tgtggcacgc 450

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 88  
 LENGTH: 98  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 88  
 Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln  
     1                    5                    10                    15  
 Val. . . . . Gln Ile Asp Asp Gly Ala Ala Gly Val  
                     85                    90                    95

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 89  
 LENGTH: 460  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 89  
 gcaaccggct ttctgatcag ctgagacatc agcggcgtgc gggtaacga cccacctgcg 60  
 ccaggtagcg actccgcgcg cagcaggccc gcgccgcgc tggggcctga tccaccagcc 120  
 agcggatggt tcgacagcgg actggtgccg agcaggccca tctgcgcggc ttctctgctc 180  
 gctgggttgc cgccgccggt. . . . . gggagggcat tccgaagatc 360  
 gggttcgtcg tgctctggct cgcgccggga tcaaggatcg acgccatcgg ctcgagcttc 420  
 tcgaaaagcg tgtaaccgc ggtctcggcc tggtagacct 460

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 90  
 LENGTH: 139  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 90  
 Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser  
     1                    5                    10                    15  
 Arg. . . . . 125  
 Ser Lys Ser Val Leu Thr Ala Val Ser Ala Trp  
     130                    135

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 91  
 LENGTH: 1200

TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 91  
 taataggccc ccaacacatc ggagggagtg atcaccatgc tgtggcacgc aatgccaccg 60  
 gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120  
 gcgggatggc agacgctttc ggcggctctg gacgtcagg ccgtcgagtt gaccgcgcgc 180  
 ctgaactctc tgggagaagc. . . 1080  
 ccgctcgcgc aggagcgtga agaagacgac gaggacgact gggacgaaga ggacgactgg 1140  
 tgagctcccg taatgacaac agacttcccg gccacccggg ccggaagact tgccaacatt 1200

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 92

LENGTH: 371

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 92

Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala

1 5 10 15

Arg. . . Glu Asp Asp Trp Asp Glu Glu

355 360 365

Asp Asp Trp

370

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 93

LENGTH: 1000

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 93

gacgcgacac agaaatcctt aaggccggcg gccaaagggc cgaaggtgaa gaaggtgaag 60

ccccagaaac cgaaggccac gaagccggcc aaagtgggtg cgcagcgcg ctggcgacat 120

tgggtgcatg cgttgacgcg aatcaacctg ggcctgtcac ccgacgagaa gtacgagctg 180

gacctgcacg ctcgagtccg. . . cactcgactt gctcgaccct 900

atctacaagc gcaaggtcct cgaattggcc gcagcgctat ccgacgattt cgagagggct 960

ggacgtcggt gagcgcacct gctgttgctg ctggtcctac 1000

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 94

LENGTH: 308

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 94

Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys

1 5 10 15

Val. . . Leu Ser Asp Asp Phe Glu Arg

290 295 300

Ala Gly Arg Arg

305

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 95

LENGTH: 34

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 95

aagagtagat ctatgatggc cgaggatgtt cgcg 34

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 96

LENGTH: 27

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 96

cgcgacgac ggatcctacc gcgtcgg 27

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 97

LENGTH: 28

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 97

ccttgggaga tctttggacc ccggttgc 28

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 98

LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 98  
 gacgagatct tatgggctta ctgac 25  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 99  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 99  
 ccccccagat ctgcaccacc ggcacgcggcg ggc 33  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 100  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 100  
 gcggcggatc cggttgcttag ccgg 24  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 101  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 101  
 ccggctgaga tctatgacag aatacgaagg gc 32  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 102  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 102  
 ccccgccagg gaactagagg cggc 24  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 103  
 LENGTH: 38  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 103  
 ctgccgagat ctaccaccat tgtcgcgctg aaataccc  
 DETD 38  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 104  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 104  
 cgccatggcc ttacgcgcca actcg 25  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 105  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 105  
 ggcgagatc tgtgagtttt ccgtatttca tc 32  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 106  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 106  
 cgcgtcgagc catgggtagg cgcag 25  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 107  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 107

gaggaagatc tatgacaact tcacccgacc cg	32
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 108	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 108	
catgaagcca tggcccgag gctgcatg	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 109	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 109	
ggccgagatc tgtgaccac tatgacgtcg tcg	33
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 110	
LENGTH: 36	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 110	
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc	36
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 111	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 111	
ccgggagatc tatggcaaag ctctccaccg acg	33
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 112	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 112	
cgctgggcag agctacttga cggtgacggt gg	32
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 113	
LENGTH: 36	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 113	
ggcccagatc tatggccatt gaggtttcgg tgttgc	36
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 114	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 114	
cgccgtgttg catggcagcg ctgagc	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 115	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 115	
ggacgttcaa gcgacacatc gccg	24
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 116	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 116	
cagcacgaac gcgccgtcga tggc	24
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 117	
LENGTH: 26	
TYPE: DNA	

ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 117	
acagatctgt gacggacatg aacccg	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 118	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 118	
ttttccatgg tcacgggccc ccgtact	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 119	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 119	
acagatctgt gcccatggca cagata	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 120	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 120	
tttaagcttc taggcgcca gcgcggc	27
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 121	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 121	
acagatctgc gcatgcggat ccgtgt	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 122	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 122	
ttttccatgg tcatccggcg tgatcgag	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 123	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 123	
acagatctgt aatggcagac tgtgat	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 124	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 124	
ttttccatgg tcaggagatg gtgatcga	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 125	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 125	
acagatctgc cggctacccc ggtgcc	26
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 126	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 126	
ttttccatgg ctattgcagc ttccggc	28
SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 127	

LENGTH: 50  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 127  
 Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5 10 15  
 Val. . . Val Leu Ala Glu Ala Ala Gly Thr  
 35 40 45  
 Val Ser  
 50

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 128

LENGTH: 49

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 128

Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5 10 15

Val. . . Pro Val Leu Ala Glu Ala Ala Gly Thr Val  
 35 40 45

Ser

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 129

LENGTH: 50

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 129

Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
 1 5 10 15

Val. . . Val Leu Ala Glu Ala Ala Gly Thr  
 35 40 45

Val Ser

50

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 130

LENGTH: 33

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 130

ccgggagatc tatggcaaag ctctccaccg acg 33

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 131

LENGTH: 32

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 131

cgctgggcag agctacttga cggtgacggt gg 32

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 132

LENGTH: 36

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 132

ggcgccggca agcttgccat gacagagcag cagtgg 36

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 133

LENGTH: 26

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 133

cgaactcgcc ggatcccgtg tttcgc 26

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 134

LENGTH: 32

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 134

ggcaaccgcg agatctttct cccggccggg gc 32

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 135

LENGTH: 27

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 135

ggcaagcttg ccggcgcccta acgaact

27

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 136

LENGTH: 30

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 136

ggacccagat ctatgacaga gcagcagtgg

30

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 137

LENGTH: 47

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 137

ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg

47

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 138

LENGTH: 44

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 138

gttcgcaaag cttttctccc ggccggggct gccggctcgag tacc

44

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 139

LENGTH: 20

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 139

ccttcggttg atcccgtcag

20

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 140

LENGTH: 450

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 140

tggcgctgtc accgaggaac ctgtcaatgt cgctcgagcag tactgaaccg ttccgagaaa 60

ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120

gaagagtgtc tcggccagcg gcgatacctt gggtgccgctc atcagcgacc tggaggccaa 180

ctattcgggc atttccgagc. . . cgccgtggcc ggtgggtgag cggagcacat 360

gacacgatac gactcgctgt tgcaggcctt gggcaacacg ccgctgggtg gctgcagcg 420

attgtcgcca cgctgggatg acgggcgaga 450

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 141

LENGTH: 93

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 141

Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly

1 5 10 15

Gly. . . Ser Val Thr Ile Leu Pro Ala Val Ala Gly Gly

85 90

## SEQUENCE CHARACTERISTICS:

SEQ ID NO: 142

LENGTH: 480

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 142

gggtgttccc cggccgggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60

tccaggttca acaaggagac aggcaacatg gcaacacggt ttatgacgga tccgcacgcg 120

atgcgggaca tggcggggccg ttttgagggtg cacgcccaga cgggtggagga cgagggtcgc 180

cggatgtggg cgctccgcgca. . . 360

tcccagcaga tcctcagcag ctaacgtcag ccgctgcagc acaatacttt tacaagcgaa 420

ggagaacagg ttcgatgacc atcaactatc agttcgggtga tgtcgacgct catggcgcca 480

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 143

LENGTH: 98

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 143

Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala

1 5 10 15

Gly. . . Gln Glu Gln Ala Ser Gln Gln Ile Leu

85 90 95

Ser Ser

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 144

LENGTH: 940

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 144

gccccagttcc tccgatcgctt catcgcttcc accggccgcc agccgaccgc agggccacgtg 60

tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120

gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct acacatcggt 180

gttcggctgg gggtacgacg. . . gatccgcagg gcgcgatctt 840

cagtgtgttg aagcccgcc cgcagcaata gggagcatcc cgggcaggcc cgccggccgg 900

cagattcgga gaatgctaga agctgccgcc ggcgccgccg 940

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 145

LENGTH: 261

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 145

Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp

1 5 10 15

Leu. . . Phe Ser Val Leu Lys

245 250 255

Pro Ala Pro Gln Gln

260

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 146

LENGTH: 280

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 146

ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacagggaac 60

tgtgaagtgg ttcaacgcgg agaaggggtt cggctttatc gccccgaag acggttccgc 120

ggatgtattt gtccactaca cggagatcca gggaaacggc ttccgcaccc ttgaagaaaa 180

ccagaaggtc gagttcgaga tcggccacag ccctaagggc cccagggcca ccggagtccg 240

ctcgctctga gttacccccg cgagcagacg caaaaagccc 280

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 147

LENGTH: 67

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 147

Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly

1 5 10 15

Phe. . . Gly Pro Gln Ala Thr Gly Val

50 55 60

Arg Ser Leu

65

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 148

LENGTH: 540

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 148

atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60

acttcgtgtc ccaaatgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120

atcagaccct gacgctgcga ctgctggcgg catccgcggg cattctcagc gccgcggcct 180

tcgccgcgcc agcacaggca. . . 420  
cctcggatgat ggcagacgtc gccagcggca acctgccggc cctgccagac atgccggggc 480  
tgcccgggtc ctaggcgtgc gcggctccta gccggtcctt aacggatcga tcgtggatgc 540

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 149

LENGTH: 129

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 149

Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala  
1 5 10 15

Ser. . . Ala Leu Pro Asp Met Pro Gly Leu Pro Gly  
115 120 125

Ser

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 150

LENGTH: 400

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 150

atagtttggg gaaggtgtcc ataaatgagg ctgtcgttga ccgcattgag cgccggtgta 60  
ggcgccgtgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120  
gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa cgcgacggat 180  
ccgggggctg ccgcacagtt. . . aattgcaagc tgtgccgggg 300  
gcggcacagt acatcggcct tgtcgagtcg gttgccggct cctgcaacaa ctattaagcc 360  
catgccggcc ccacccgcg acccggcatc gtcgccgggg 400

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 151

LENGTH: 110

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 151

Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala  
1 5 10 15

Met. . . Glu Ser Val Ala Gly Ser Cys Asn Asn Tyr  
100 105 110

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 152

LENGTH: 990

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 152

aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga gggtccgcag tcgagcgctg 60  
cgggccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120  
aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg ctggaccgcg 180  
aggccgccga cgcggtgctg. . . tggttgccca gaaaatcatc taagacatac 900  
gcacctccca aagacgagag cgatataacc catggctgaa gtactggtgc tcgttgagca 960  
cgctgaaggc gcgttaaaga aggtcagcgc 990

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 153

LENGTH: 266

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 153

Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser  
1 5 10 15

Glu. . . 250 255  
Val Gln Tyr Leu Val Ala Gln Lys Ile Ile  
260 265

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 154

LENGTH: 25

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 154

ctgagatcta tgaacctacg gcgcc

SEQUENCE CHARACTERISTICS:

SEQ ID NO: 155

LENGTH: 35  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 155  
 ctcccatggt accctaggac ccgggcagcc ccggc 35  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 156  
 LENGTH: 29  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 156  
 ctgagatcta tgaggctgtc gttgaccgc 29  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 157  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 157  
 ctccccgggc ttaatagttg ttgcaggagc 30  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 158  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 158  
 gcttagatct atgattttct gggcaaccag gta 33  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 159  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 159  
 gcttccatgg gcgaggcaca ggcgtgggaa 30  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 160  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 160  
 ctgagatcta gaatgccaca gggaactgtg 30  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 161  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 161  
 tctcccgggg gtaactcaga gcgagcggac 30  
 SEQUENCE CHARACTERISTICS:  
 SEQ  
 DETD ID NO: 162  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 162  
 ctgagatcta tgaacgtcac cgtatcc 27  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 163  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 163  
 tctcccgggg ctcacccacc ggccacg 27  
 SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 164  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 164

ctgagatcta tggcaacacg ttttatgacg 30  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 165  
LENGTH: 30  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 165

ctccccgggt tagctgctga ggatctgcth 30  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 166  
LENGTH: 31  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 166

ctgaagatct atgccaaga gaagcgaata c 31  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 167  
LENGTH: 31  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 167

cggcagctgc tagcattctc cgaatctgcc g 31  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 168  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 168  
Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly  
1 5 10 15  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 169  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
FEATURE:  
NAME/KEY: UNSURE  
LOCATION: (15)  
OTHER INFORMATION: Xaa is unknown  
SEQUENCE: 169  
Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa Xaa Xaa  
1 5 10 15  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 170  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
FEATURE:  
NAME/KEY: VARIANT  
LOCATION: (1)  
OTHER INFORMATION: Thr could also be Ala  
SEQUENCE: 170  
Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala Gly  
1 5 10 15  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 171  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 171  
Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp  
1 5 10 15  
SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 172  
LENGTH: 404  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 172

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His  
 1 5 10 15  
 Ile. . . Ser Thr Glu Gly Asn Val Thr  
 385 390 395 400

Gly Met Phe Ala

# SEQUENCE CHARACTERISTICS:

SEQ ID NO: 173

LENGTH: 403

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 173

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His  
 1 5 10 15

Ile.

CLM What is claimed is:

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) consists essentially of an amino acid sequence with a sequence identity of at least 80% with SEQ.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; wherein "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length, . . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length, . . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length, . . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . weeks of primary infection or within 4 days after the mouse has been re-challenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml, . . .

. . . with respect to the ability of evoking a protective immune in mice response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length, . . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the

**tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, and "sequence identity" is a measure of the degree of similarity between two amino acid sequences of equal length, . . . .

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . with respect to the ability of evoking a protective immune response in mice against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex.

. . . weeks of primary infection or within 4 days after the mouse has been re-challenge infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml, . . . suspension; and/or c) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

32. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any one of claims 1 or 2 optionally. . . .

43. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any one of claims 3 or 4 optionally. . . .

L13 ANSWER 8 OF 10 USPATFULL on STN

AN 2002:314395 USPATFULL

TI Hybrids of M. **tuberculosis** antigens

IN Andersen, Peter, Bronshoj, DENMARK

Olsen, Anja Weinreich, Soborg, DENMARK

Skjot, Rikke Louise Vinther, Hedehusene, DENMARK

Rasmussen, Peter Birk, Frederiksberg, DENMARK

PI US 2002176867 A1 20021128

AI US 2001-805427 A1 20010313 (9)

RLI Continuation-in-part of Ser. No. US 1998-246191, filed on 30 Dec 1998, ABANDONED

PRAI DK 1997-1277 19971110

US 1998-70488P 19980105 (60)

US 1997-44624P 19970418 (60)

DT Utility

FS APPLICATION

LREP Thomas J. Kowalski, c/o FROMMER LAWRENCE & HAUG LLP, 745 Fifth Avenue,  
New York, NY, 10151  
CLMN Number of Claims: 25  
ECL Exemplary Claim: 1  
DRWN 10 Drawing Page(s)  
LN.CNT 2157

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention discloses fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** vaccine based on the fusion proteins, which vaccine induces efficient immunological memory.

TI Hybrids of M. **tuberculosis** antigens

AB The present invention discloses fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** vaccine based on the fusion proteins, which vaccine induces efficient immunological memory.

SUMM [0003] The present application discloses new fusion proteins of the immunodominant antigens ESAT-6 and Ag85B from Mycobacterium **tuberculosis** or homologues thereof, and a **tuberculosis** subunit vaccine comprising at least one fusion protein. The vaccine induced efficient immunological memory.

SUMM [0004] Human **tuberculosis** caused by Mycobacterium **tuberculosis** (M. **tuberculosis**) is a severe global health problem, responsible for approx. 3 million deaths annually, according to the WHO. The worldwide incidence of new **tuberculosis** (TB) cases had been falling during the 1960s and 1970s but during recent years this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. **tuberculosis**.

SUMM [0007] Immunity to M. **tuberculosis** is characterized by some basic features; specifically sensitized T lymphocytes mediates protection, and the most important mediator molecule seems to.

SUMM [0008] M. **tuberculosis** holds, as well as secretes, several proteins of potential relevance for the generation of a new TB vaccine. For a.

SUMM [0009] Animal **tuberculosis** is caused by Mycobacterium bovis, which is closely related to M. **tuberculosis** and within the **tuberculosis** complex. M. bovis is an important pathogen that can infect a range of hosts, including cattle and humans. **Tuberculosis** in cattle is a major cause of economic loss and represents a significant cause of zoonotic infection. A number of.

SUMM . . . A. D. et al 1995), genetic immunization (Huygen et al 1996, Tascon et al 1996) and attenuated strains of M. **tuberculosis** (Guleria et al 1996) are currently being explored in many laboratories. Due to the complexity of the host immune response against **tuberculosis** and the genetic restriction imposed by major histocompatibility complex molecules (MHC), it has become clear that an effective subunit vaccine.

SUMM . . . a significant level of anti-TB protection expressed as a reduction of bacterial numbers in organs of mice challenged with M. **tuberculosis** by the aerosol or i.v route. There is a long held debate whether the bacterial load in various organs uniformly correlates with the ultimate outcome of **tuberculosis** infection, especially in animals vaccinated with experimental TB vaccines (Wiegshaues, E. H. et al 1970, Baldwin, S. L. et al.

SUMM [0015] Recent international focus on TB vaccine research and the sequencing of the M. **tuberculosis** genome (Cole et al 1998) have resulted in the accelerated identification of novel mycobacterial proteins. Culture filtrates have attracted particular.

SUMM . . . adoptively transfer immunity to recipient mice as late as 22 weeks after vaccination with a mixture of DDA and M. **tuberculosis** culture filtrate (Andersen, P. 1994)

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B and/or a stretch of amino acids which protects the first amino acid sequence

from in vivo degradation or.

SUMM [0025] A preferred polypeptide within the present invention is an immunogenic antigen from *M. tuberculosis*. Such antigen can for example be derived from *M. tuberculosis* and/or *M. tuberculosis* culture filtrate. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native *M. tuberculosis* antigen or be heterologous and such sequences may, but need not, be immunogenic.

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the *tuberculosis* complex or a virulent mycobacterium. This can be accomplished by preparing the polypeptide by means of recombinant methods in a . . .

SUMM [0028] By the term "virulent mycobacterium" is understood a bacterium capable of causing the *tuberculosis* disease in an animal or in a human being. Examples of virulent mycobacteria are *M. tuberculosis*, *M. africanum*, and *M. bovis*. Examples of relevant animals are cattle, possums, badgers and kangaroos.

SUMM [0045] In the context of providing candidate molecules for a new vaccine against *tuberculosis*, the subdominant epitopes are however as relevant as are the dominant epitopes since it has been show (Olsen et al. . . .

SUMM . . . be determined by the use of T cell lines derived from an immune individual or a person infected with *M. tuberculosis* where the T cell lines have been driven with either live mycobacteria, extracts from the bacterial cell or culture filtrate. . . .

SUMM [0054] In general, *M. tuberculosis* antigens, and DNA sequences encoding such antigens, may be prepared using any one of a variety of procedures. They may be purified as native proteins from the *M. tuberculosis* cell or culture filtrate by procedures such as those described above. Immunogenic antigens may also be produced recombinantly using a . . .

SUMM . . . at least one fusion partner. The fusion partner can, in order to enhance immunogenicity, be another polypeptide derived from *M. tuberculosis*, such as of a polypeptide fragment derived from a bacterium belonging to the *tuberculosis* complex, such as TB10.4, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, MPB64, MPT64, Ag85A, MPB59, Ag85C, 19 kDa lipoprotein, MPT32 and alpha-crystallin, or at least one T-cell epitope of. . . .

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other *M. tuberculosis* antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . Nature 400: 269-71). Antigens with therapeutic properties may be identified based on their ability to diminish the severity of *M. tuberculosis* infection in experimental animals or prevent reactivation of previous infection, when administered as a vaccine. The composition used for therapeutic. . . .

DRWD [0080] FIG. 1. SDS-PAGE analysis of purified recombinant *M. tuberculosis* antigens. 1 µg of protein was loaded in each lane. Lane 1: molecular weight standard; Lane 2: recombinant ESAT-6; Lane. . . .

DRWD . . . with the adjuvant alone were included. Ten weeks after the first vaccination, the mice received an aerosol challenge with *M. tuberculosis* Erdman and the numbers of bacteria (CFU's) were quantified in the lungs and spleens 6 weeks later. The values are. . . .

DRWD [0084] FIG. 5. Dynamics of mortality in *M. tuberculosis* -infected mice. Groups of 6-12 mice were vaccinated s.c. with either protein-based vaccines or live BCG as described in the example and challenged with a standard lethal dose of 5+10<sup>sup</sup>.5 *M. tuberculosis* H37Rv CFUs. Numbers in parentheses indicate the mean survival time (MST±SEM) in days.

DRWD [0085] FIG. 6. Body weights of guinea pigs aerosol-infected with *M. tuberculosis*. The guinea pigs were either vaccinated with BCG, Ag85B-ESAT-6, or adjuvant-control (n=6). Data are depicted in grams. \*, euthanized because. . . .

DRWD [0086] FIG. 7. Proliferation of *M. tuberculosis*-specific human T cell lines (A-I) with different HLA-DR types in response to ESAT-6, Ag85B and the fusion proteins. Data are.

DRWD [0088] FIG. 9. Mean weight loss in vaccinated and unvaccinated cynomolgous monkeys 12 weeks after intratracheal infection with *M. tuberculosis*.

DRWD FIG. 10. Vaccine efficacy in vaccinated cynomolgous monkeys (n=3) compared to unvaccinated controls, 12 weeks after intratracheal infection with *M. tuberculosis*. Protection is expressed as the log of the mean difference between the number of bacteria detected in the lungs of.

DETD compared to the strong recognition of the antigen that has been found during the recall of memory immunity to *M. tuberculosis*. ESAT-6 has been found in ST-CF in a truncated version where amino acids 1-15 have been deleted. The deletion includes.

DETD [0100] PCR reactions contained 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer).

DETD [0116] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57BI/6j mice with 5+10.sup.4 *M. tuberculosis* i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were.

DETD used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10.sup.6 *M. tuberculosis* i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive.

DETD [0119] The skin test activity of the purified proteins was tested in *M. tuberculosis* infected guinea pigs.

DETD [0120] 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of *M. tuberculosis* H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was.

DETD TB infection in different animal models.

TABLE 1

DTH erythema diameter in guinea pigs i.v. infected with 1 + 10.sup.4 CFU *M. tuberculosis*, after stimulation with 10 µg antigen.

Antigen	Mean (mm)	SEM
PBS	3.25	0.48
PPD (2TU)	10.88	1
Ag85B-ESAT6	14.75	1.5

The values.

DETD and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 *M. tuberculosis* suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were.

DETD female C57BLU6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 *M. tuberculosis* suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

DETD (H2.sup.k) A.SW (H2.sup.s)

Ag85B-ESAT6	+++	+++	+++	++
ESAT6-Ag85B	+++	-	+	-

Mouse IFN-γ release 14 days after primary infection with *M. tuberculosis*.

--: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.

n.d. = not determined.

DETD [0130] Mouse IFN- $\gamma$  release during recall of memory immunity to M. **tuberculosis**. --: no response; +: 1/3 of ST-CF; ++: 2/3 of ST-CF; +++: level of ST-CF.

DETD . . . donors with no known ex-posure to patients with TB and from patients with culture or microscopy proven infection with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD [0149] M. **tuberculosis** Erdman and H37Rv was grown at 37° C. in modified Sauton medium enriched with 0.5% sodium pyruvate and 0.5% glucose.. . .

DETD [0151] Recombinant Ag85B was produced as follows: The coding region of ag85B was amplified by PCR from M. **tuberculosis** H37Rv chromosomal DNA with the following primer sets:

OPBR-77: GTTCGCAAAGCTTTTCTCCCGGCCGGGGCTGCCGGTCGAGTACC  
(SEQ ID NO:11)

HindIII

NO:11)

DETD . . . the production of recombinant Ag85B, the coding region (without the secretory signal sequence) of Ag85B was PCR amplified from M. **tuberculosis** H37Rv chromosomal DNA using Ag85B-F1 and Ag85B-R2 primers. A unique BamHI site was introduced by the Ag85B-R2 primer. The PCR. . .

DETD . . . immunization either by the aerosol route in a Glas-Col inhalation exposure system, calibrated to deliver approximately 100 CFUs of M. **tuberculosis** Erdman/lung or by the i.v. route with an inoculum of 5+10<sup>sup</sup>.4 CFU of M. **tuberculosis** (H37Rv) suspended in PBS in a volume of 0.2 ml. Mice were sacrificed 6 weeks (aerosol route) or 2 weeks. . .

DETD . . . naive mice were included as controls. Ten weeks after the first immunization, the mice received an aerosol challenge with M. **tuberculosis** Erdman. FIG. 3 shows the number of bacteria in lungs and spleens expressed as mean log.sub.10 CFU. Even with a. . .

DETD . . . mice were challenged by the aerosol (Exp. 1 and 2) or by the i.v (Exp 3) route with virulent M. **tuberculosis**. Six (Exp. 1 and 2) or two weeks (Exp. 3) post challenge, the mice were killed and the bacterial numbers. . .

DETD . . . included naive mice, BCG-vaccinated mice and a group of mice receiving the adjuvant alone. Mice were aerosol challenged with M. **tuberculosis** Erdman 10 and 30 weeks after the first vaccination. Both the fusion protein and BCG induced significant and similar levels. . . was observed after a longer rest period (30 weeks) and both vaccines induced long-lived memory immunity, which protected efficiently against **tuberculosis**. However, whereas the subunit vaccine promoted a stable level of protective immunity over the observation period, the efficacy of BCG. . . injected three times with the experimental vaccines emulsified in MPL-DDA.

.sup.bBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis**  $\pm$  SEM (n = 5) isolated from the spleen and lung 6 weeks post aerosol challenge (Exp. 1 and Exp. . . .

DETD . . . injected three times with the experimental vaccines emulsified in MPL-DDA.

.sup.bBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis**  $\pm$  SEM (n = 4-5) isolated from the spleen and lung 6 weeks post aerosol challenge.

.sup.cIn Exp 2 the. . .

DETD [0174] M. **tuberculosis** Erdman and H37Rv were grown at 37° C. in modified Sauton medium enriched with 0.5% sodium pyruvate and 0.5% glucose. . . .

DETD . . . long-term survival, mice were challenged intravenously 6 wk following the last immunization with a lethal dose of 5+10<sup>5</sup> CFU M. **tuberculosis** H37Rv. Three weeks following infection, 3 mice per group were sacrificed and CFU counts in organs were determined by plating. . . .

DETD [0186] Guinea pigs were challenged 12 weeks after the initial vaccination in either a Glas-Col inhalation exposure system with M.

**tuberculosis** Erdman (the SSI experiment 1) or using a contained Henderson apparatus (The CAMR experiment 2) as previously described (9); Williams, . . .

DETD [0189] Protection Against Death from M. **tuberculosis** Infection in Ag85B-ESAT-6 Fusion Protein Vaccinated Mice

DETD . . . the lung at this time-point. Severe loss of body weight, or wasting, is a common and well-described clinical symptom in **tuberculosis** patients (Prout, S. et al 1980). Hence, we monitored the body weight as a potentially important parameter of M. **tuberculosis**-triggered disease in guinea pigs (FIG. 6). When the guinea pigs had lost 20% of maximum weight or, if showing other. . .

DETD . . . derived from 7 TB patients and 2 PPD-converters representing 8 different HLA-DR phenotypes. The T cell lines raised against M. **tuberculosis** were tested with respect to their ability to specifically proliferate in the presence of ESAT-6, Ag85B and the fusion protein. . .

DETD . . . regarded positive. Responses to PBS were less than 5 mm. .sup.cBacterial numbers are given as mean log.sub.10 CFU of M. **tuberculosis** ± SEM (n = 5-6) isolated from the spleen and lung. .sup.dNA, not available, due to severe disease, they were. . .

DETD . . . to subsequent in vitro rechallenge of lymphocytes with the vaccine. Vaccinated animals show significant protection against aerosol infection with M. **tuberculosis** as well as reduced pathology and weight loss, see FIGS. 8-10.

DETD [0227] Patent application PA 2000 00666 (our ref. 22030 DK1) "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0228] U.S. patent application No. 09/0505,739 "Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**"

DETD [0229] Patent application WO 01/04151 (our ref.23388 DK1) "**Tuberculosis** vaccine and diagnostic based on the Mycobacterium **tuberculosis** esat-6 gene family".

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 1

LENGTH: 95

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 1

Met Thr Glu Gln Gln Trp Asn Phe Ala Gly Ile Glu Ala Ala Ala Ser

1 . . . . . 5 . . . . . 10. . . . .

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 2

LENGTH: 325

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: SIGNAL

LOCATION: (1)..(40)

SEQUENCE: 2

Met Thr Asp Val Ser Arg Lys Ile Arg Ala Trp Gly Arg Arg Leu Met

1. . . . .

CLM What is claimed is:

. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising. . .

. . . for the preparation of a pharmaceutical composition, e.g. for the vaccination against infections caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

. . . to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to **tuberculosis** caused by virulent mycobacteria, e.g. by

Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, in an animal, including a human being.  
a nucleic acid fragment according to claim 12 or 13 for the preparation of a composition for the diagnosis of **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

nucleic acid fragment according to claim 12 or 13 for the preparation of a pharmaceutical composition for the vaccination against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis.

18. A vaccine for immunizing an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a.

the polypeptide from the host cell or culture medium; (b) isolating Ag85B and ESAT-6 from a whole mycobacterium, e.g. Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, from culture filtrate or from lysates or fractions thereof, and fusing the polypeptides; (c) synthesizing.

22. A method for immunising an animal, including a human being, against **tuberculosis** caused by virulent mycobacteria, e.g. by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis, comprising administering to the animal the polypeptide according to claim 1, the immunogenic composition according.

first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising.

first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein Ag85B, said first and second amino acid sequences optionally being fused via a linker sequence; (b) a polypeptide comprising.

L13 ANSWER 9 OF 10 USPATFULL on STN

AN 2002:178550 USPATFULL

TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**

IN Andersen, Peter, Bronshoj, DENMARK

Nielsen, Rikke, Frederiksberg C, DENMARK

Oettinger, Thomas, Hellerup, DENMARK

Rasmussen, Peter Birk, Kobenhaven O, DENMARK

Rosenkrands, Ida, Kobenhaven O, DENMARK

Weldingh, Karin, Kobenhaven N, DENMARK

Florio, Walter, Frederiksberg C, DENMARK

PA STATENS SERUM INSTITUT (non-U.S. corporation)

PI US 2002094336 A1 20020718

AI US 2001-791171 A1 20010220 (9)

RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING

PRAI DK 1997-376 19970402

DK 1997-1277 19971110

US 1997-44624P 19970418 (60)

US 1998-70488P 19980105 (60)

DT Utility

FS APPLICATION

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CLMN Number of Claims: 53

ECL Exemplary Claim: 1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

TI Nucleic acid fragments and polypeptide fragments derived from *M. tuberculosis*

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, . . . . .

SUMM [0001] The present invention relates to a number of immunologically active, novel polypeptide fragments derived from the *Mycobacterium tuberculosis*, vaccines and other immunologic compositions containing the fragments as immunogenic components, and methods of production and use of the polypeptides. The invention also relates to novel nucleic acid fragments derived from *M. tuberculosis* which are useful in the preparation of the polypeptide fragments of the invention or in the diagnosis of infection with *M. tuberculosis*. The invention further relates to certain fusion polypeptides, notably fusions between ESAT-6 and MPT59.

SUMM [0002] Human *tuberculosis* (hereinafter designated "TB") caused by *Mycobacterium tuberculosis* is a severe global health problem responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence. . . . has markedly changed this trend due to the advent of AIDS and the appearance of multidrug resistant strains of *M. tuberculosis*.

SUMM [0005] Immunity to *M. tuberculosis* is characterized by three basic features; i) Living bacilli efficiently induces a protective immune response in contrast to killed preparations;. . . .

SUMM [0006] Short term-culture filtrate (ST-CF) is a complex mixture of proteins released from *M. tuberculosis* during the first few days of growth in a liquid medium (Andersen et al., 1991). Culture filtrates has been suggested. . . .

SUMM . . . . invention is i.a. based on the identification and characterization of a number of previously uncharacterized culture filtrate antigens from *M. tuberculosis*. In animal models of TB, T cells mediating immunity are focused predominantly to antigens in the regions 6-12 and 17-30. . . . the Sanger Database (cf. below) with the genes encoding CFP21 and CFP25, (cfp25 and cfp21 respectively), shows homology to two *M. tuberculosis* DNA sequences, orf19A and orf23. The two sequences, orf19A and orf23, encode to putative proteins CFP19A and CFP23 with the. . . .

SUMM [0011] The present invention is also based on the identification of a number of putative antigens from *M. tuberculosis* which are not present in *Mycobacterium bovis* BCG strains. The nucleotide sequences encoding these putative antigens are: rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, **rdl-orf5**, rdl-orf9a, and rdl-orf9b.

SUMM . . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the *tuberculosis* complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the *tuberculosis* complex, or

SUMM . . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the *tuberculosis* complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or

ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex,

SUMM . . . any other antigen with which it is natively associated, i.e. free of any other antigen from bacteria belonging to the **tuberculosis** complex. This can be accomplished by preparing the polypeptide fragment by means of recombinant methods in a non-mycobacterial host cell.

SUMM . . . and any one of 168-171 denotes any continuous stretch of at least 6 amino acid residues taken from the M. **tuberculosis** derived polypeptides in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, any one of 17-23, 42, 48, . . . being immunological equivalent thereto with respect to the ability of conferring increased resistance to infections with bacteria belonging to the **tuberculosis** complex. Thus, included is also a polypeptide from different sources, such as other bacteria or even from eukaryotic cells.

SUMM . . . in a guinea pig and/or in a primate such as a human being against infections with bacteria belonging to the **tuberculosis** complex which is at least 20% of the acquired increased resistance conferred by Mycobacterium bovis BCG and also at least . . . other organ homogenates isolated from the mouse or guinea pig receiving a challenge infection with a virulent strain of M. **tuberculosis**, or, in a primate such as a human being, being assessed by determining the protection against development of clinical **tuberculosis** in a vaccinated group versus that observed in a control group receiving a placebo or BCG (preferably the increased resistance. . .

SUMM . . . diagnostically significant immune response in a mammal indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex; this diagnostically significant immune response can be in the form of a delayed type hypersensitivity reaction which can e.g. . .

SUMM . . . isolated from the experimental animal which have received a challenge infection with a virulent strain of mycobacteria belonging to the **tuberculosis** complex after previously having been immunized with the polypeptide, as compared to the mycobacterial counts in a control group of experimental animals infected with the same virulent strain, which experimental animals have not previously been immunized against **tuberculosis**. The comparison of the mycobacterial counts may also be carried out with mycobacterial counts from a group of experimental animals. . .

SUMM . . . the ability of the polypeptide fragment of the invention to confer increased resistance is to compare the incidence of clinical **tuberculosis** in two groups of individuals (e.g. humans or other primates) where one group receives a vaccine as described herein which.

SUMM [0033] The "**tuberculosis**-complex" has its usual meaning, i.e. the complex of mycobacteria causing TB which are Mycobacterium **tuberculosis**, Mycobacterium bovis, Mycobacterium bovis BCG, and Mycobacterium africanum.

SUMM . . . other short peptide sequences), whereas the product which can be isolated from short-term culture filtrates from bacteria belonging to the **tuberculosis** complex are free of these sequences. Although it may in some applications be advantageous to produce these polypeptides recombinantly and. . .

SUMM . . . weeks of primary infection or within 4 days after the mouse has been rechallenged infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200,000 spleen cells per ml, . . .

SUMM [0050] 3) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

SUMM . . . as to allow for multiple expression of relevant epitopes), and an other polypeptide derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6, MPB64, MPT64, and MPB59 or at least one T-cell epitope of any of these antigens. Other. . .

SUMM . . . first amino acid sequence including at least one stretch of amino acids constituting a S-cell epitope derived from the M. **tuberculosis** protein ESAT-6 or MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 (if the first stretch of amino acids are derived from ESAT-6) or MPT59 (if the first.

SUMM . . . one, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide (the "parent" polypeptide) selected from the group consisting of a polypeptide fragment according to the present invention and described. . . detail above and in the examples, or the amino acid sequence could be derived from any one of the M. **tuberculosis** proteins DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin.

SUMM [0078] isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions, or

SUMM . . . interesting are rapid-growing mycobacteria, e.g. M. smegmatis, as these bacteria have a high degree of resemblance with mycobacteria of the **tuberculosis** complex and therefore stand a good chance of reducing the need of performing post-translational modifications of the expression product.

SUMM . . . been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

SUMM . . . in an immune diagnostic agent due to their extracellular presence in culture media containing metabolizing virulent mycobacteria belonging to the **tuberculosis** complex, or because of their high homologies with such extracellular antigens, or because of their absence in M. bovis BCG.

SUMM . . . to the invention, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance.

SUMM . . . defined above, or some but not all of the peptides may be derived from a bacterium belonging to the M. **tuberculosis** complex. In the latter example the polypeptides not necessarily fulfilling the criteria set forth above for polypeptides may either act.

SUMM . . . which is a vaccine for immunizing an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis**-complex, comprising as the effective component a microorganism, wherein one or more copies of a DNA sequence encoding a polypeptide as.

SUMM [0116] The invention also relates to a method of diagnosing TB caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide.

SUMM . . . pertains to a method for immunising an animal, including a human being, against TB caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide of the invention, or a vaccine composition of the invention as described.

SUMM . . . gene in the mycobacterial genome has been demonstrated to have a very limited distribution in other mycobacterial strains that M. **tuberculosis**, e.g. esat-6 is absent in both BCG and the majority of mycobacterial species isolated from the environment, such as M. . . the invention are especially well-suited for performing the diagnosis of on-going or previous infection with virulent mycobacterial strains of the **tuberculosis** complex, and it is contemplated that it will be possible to distinguish between 1) subjects (animal or human) which have.

SUMM . . . vitro method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from

the.

DRWD [0128] FIG. 1: Long term memory immune mice are very efficiently protected towards an infection with *M. tuberculosis*. Mice were given a challenge of *M. tuberculosis* and spleens were isolated at different time points. Spleen lymphocytes were stimulated in vitro with ST-CF and the release of.

DRWD . . . directed to molecules from 6-12 and 17-38 kDa. Splenic T cells were isolated four days after the challenge with *M. tuberculosis* and stimulated in vitro with narrow molecular mass fractions of ST-CF. The release of IFN- $\gamma$  was investigated

DRWD . . . MPB51 (Ohara et al., 1995) are underlined at position 780. The nucleotides given in italics are not present in *M. tuberculosis* H37Rv.

DETD [0135] A group of efficiently protected mice was generated by infecting 8-12 weeks old female C57Bl/6j mice with 5+10<sup>sup</sup>.4 *M. tuberculosis* i.v. After 30 days of infection the mice were subjected to 60 days of antibiotic treatment with isoniazid and were.

DETD . . . used this model to identify single antigens recognized by protective T cells. Memory immune mice were reinfected with 1+10<sup>sup</sup>.6 *M. tuberculosis* i.v. and splenic lymphocytes were harvested at day 4-6 of reinfection, a time point where this population is highly reactive.

DETD [0140] The recombinant  $\lambda$ gt11 *M. tuberculosis* DNA library constructed by R. Young (Young, R. A. et al. 1985) and obtained through the World Health Organization IMMTUB.

DETD . . . In order to obtain the nucleotide sequence of the gene encoding the pv-2 binding protein, the approximately 3 kb *M. tuberculosis* derived EcoRI--EcoRI fragment from AA242 was subcloned in the EcoRI site in the pBluescriptSK+ (Stratagene) and used to transform *E. coli*.

DETD [0150] Similarly, to obtain the nucleotide sequence of the gene encoding the st-3 binding protein, the approximately 5 kb *M. tuberculosis* derived EcoRI--EcoRI fragment from AA226 was subcloned in the EcoRI site in the pBluescriptSK+ (Stratagene) and used to transform *E. coli*.

DETD . . . sequence obtained on the insert from lambda phage AA226, a search of homology to the nucleotide sequence of the *M. tuberculosis* genome was performed in the Sanger database (Sanger Mycobacterium *tuberculosis* database):

DETD . . . in BCG are stable deletions and/or multiple mutations which do not readily revert. While physiological differences between BCG and *M. tuberculosis* and *M. bovis* has been noted, the attenuating mutations which arose during serial passage of the original BCG strain has. . . has been shown to have properties as a vaccine candidate (cf. PCT/DK94/00273 and PCT/DK/00270). In order to find new *M. tuberculosis* specific diagnostic antigens as well as antigens for a new vaccine against TB, the RD1 region (17.499 bp) of *M. tuberculosis* H37Rv has been analyzed for Open Reading Frames (ORF). ORFs with a minimum length of 96 bp have been predicted.

DETD [0177] Identification of the ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf2, rdl-orf9a, and rdl-orf9b.

DETD [0178] The nucleotide sequence of rdl-orf2 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 71. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0179] The nucleotide sequence of rdl-orf3 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 87. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0180] The nucleotide sequence of rdl-orf4 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 89. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0181] The nucleotide sequence of **rdl-orf5** from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 91. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0182] The nucleotide sequence of rdl-orf8 from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 67. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0183] The nucleotide sequence of rdl-orf9a from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 93. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0184] The nucleotide sequence of rdl-orf9b from *M. tuberculosis* H37Rv is set forth in SEQ ID NO: 69. The deduced amino acid sequence of RD1-ORF2 is set forth in.

DETD [0188] The DNA sequence **rdl-orf5** (SEQ ID NO: 91) contained an open reading frame starting with a GTG codon at position 3128-3130 and ending with.

DETD [0192] Cloning of the ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b.

DETD [0193] The ORF's rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b were PCR cloned in the pMST24 (Theisen et al., 1995) (rdl-orf3) or the pQE32 (QIAGEN) (rdl-orf2, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a and rdl-orf9b) expression vector. Preparation of oligonucleotides and PCR amplification of the rdl-orf encoding genes, was carried out as described in example 2. Chromosomal DNA from *M. tuberculosis* H37Rv was used as template in the PCR reactions. Oligonucleotides were synthesized on the basis of the nucleotide sequence from.

DETD [0200] **rdl-orf5**.

DETD [0201] A BamHI site was engineered immediately 5' of the first codon of **rdl-orf5**, and a HindIII site was incorporated right after the stop codon at the 3' end. The gene **rdl-orf5** was subcloned in pQE32, giving pT088.

DETD [0209] Purification of recombinant RD1-ORF2, RD1-ORF3, RD1-ORF4, **RD1-ORF5**, RD1-ORF8, RD1-ORF9a and RD1-ORF9b.

DETD [0211] The nucleotide sequences of rdl-orf2, rdl-orf3, rdl-orf4, **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b from *M. tuberculosis* H37Rv are set forth in SEQ ID NO: 71, 87, 89, 91, 67, 93, and 69, respectively. The deduced amino acid sequences of rdl-orf2, rdl-orf3, rdl-orf4 **rdl-orf5**, rdl-orf8, rdl-orf9a, and rdl-orf9b are set forth in SEQ ID NO: 72, 88, 90, 92, 68, 94, and 70, respectively.

DETD . . . the Linocin M18 protein from *Brevibacterium linens*, a set of degenerated primers were constructed for PCR cloning of the *M. tuberculosis* gene encoding CFP29. PCR reactions were containing 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 µM of each of the four nucleotides (Boehringer).

DETD . . . first 150 bp of this sequence was used for a homology search using the Blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0230] ([http://www.sanger.ac.uk/projects/M-tuberculosis/blast\\_server](http://www.sanger.ac.uk/projects/M-tuberculosis/blast_server)).

DETD [0231] This program identified a Mycobacterium **tuberculosis** sequence on cosmid cy444 in the database that is nearly 100% identical to the 150 bp sequence of the CFP29.

DETD . . . sequence from each of the proteins were used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD . . . protein purified from culture filtrate starts at amino acid 8 and therefore the length of the protein occurring in *M. tuberculosis* culture filtrate is 175 amino acids. This gives a theoretical molecular weigh at 18517 Da and a pI at 6.8.

DETD . . . with gene specific primers, for recombinant expression in *E. coli* of the proteins. PCR reactions contained 10 ng of *M. tuberculosis* chromosomal DNA in 1+low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides (Boehringer).

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** database:

DETD [0296] <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD . . . were found in the Sanger database. This could be due to the fact that only approximately 70% of the *M. tuberculosis* genome had been sequenced when the searches were performed. The genes encoding these proteins could be contained in the remaining.

DETD . . . CFP25, EXAMPLE 3) belong to a family of fungal cutinase homologs. Among the most homologous sequences were also two

Mycobacterium **tuberculosis** sequences found on cosmid MTCY13E12. The first, MTCY13E12.04 has 46% and 50% identity to CFP25 and CFP21 respectively. The second, . . .

DETD [0336] CFP25A: CFP25A has 95% identity in a 241 aa overlap to a putative M. **tuberculosis** thymidylate synthase 450 aa accession No p28176).

DETD [0343] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . sequence from each of the proteins was used for a homology search using the blast program of the Sanger Mycobacterium **tuberculosis** genome database:

DETD [0366] <http://www.sanger.ac.uk/projects/m-tuberculosis/TB-blast-server>.

DETD [0374] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . were used for the preparation and handling of DNA (Sambrook et al., 1989). The gene mpt51 was cloned from M. **tuberculosis** H37Rv chromosomal DNA by the use of the polymerase chain reactions (PCR) technology as described previously (Oettinger and Andersen, 1994).. .

DETD [0392] The nucleotide sequence of the cloned 952 bp M. **tuberculosis** H37Rv PCR fragment, pT052, containing the Shine Dalgarno sequence, the signal peptide sequence and the structural gene of MPT51, and. . .

DETD . . . the N-terminal region of the mature protein at position 144. Therefore, a structural gene encoding MPT51, mpt51, derived from M. **tuberculosis** H37Rv was found to be located at position 144-945 of the sequence shown in FIG. 5. The nucleotide sequence of. . .

DETD . . . compared to the strong recognition of the antigen that has been found during the recall of memory immunity to M. **tuberculosis**. ESAT-6 has been found in ST-CF in a truncated version were amino acids 1-15 have been deleted. The deletion includes. . .

DETD [0415] PCR reactions contained 10 ng of M. **tuberculosis** chromosomal DNA in 1+ low salt Taq+ buffer from Stratagene supplemented with 250 mM of each of the four nucleotides. . .

DETD . . . same high level as ST-CF.

TABLE 5

IFN- $\gamma$  release from splenic memory effector cells from C57BL/6J mice isolated after reinfection with M. **tuberculosis** after stimulation with native antigens.

Antigen.sup.a	IFN- $\gamma$ (pg/ml).sup.b
ST-CF	12564
CFP7	ND.sup.d
CFP9	ND
CFP17	9251
CFP20	2388
CFP21	10732. . .

DETD [0432] The skin test activity of the purified proteins was tested in M. **tuberculosis** infected guinea pigs.

DETD [0433] 1 group of guinea pigs was infected via an ear vein with 1+10.sup.4 CFU of M. **tuberculosis** H37Rv in 0,2 ml PBS. After 4 weeks skin tests were performed and 24 hours after injection erythema diameter was. . .

DETD . . . significant Delayed Type Hypersensitivity (DTH) reaction.

TABLE 6

DTH erythema diameter in guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**, after stimulation with native antigens.

Antigen.sup.a	Skin reaction (mm).sup.b
Control	2.00

PPD.sup.c	15.40 (0.53)
CFP7	ND.sup.e
CFP9	ND
CFP17	11.25. . .

DETD . . . animal models.

TABLE 6a

DTH erythema diameter of recombinant antigens in outbred guinea pigs infected with 1 + 10.sup.4 CFU of M. **tuberculosis**.

Antigen.sup.a	Skin reaction (mm).sup.b	
---------------	--------------------------	--

Control	2.9	(0.3)
PPD.sup.a	14.5	(1.0)
CFP 7a	13.6	(1.4)
CFP 17	6.8	(1.9)
CFP 20.		

DETD . . . and A.SW(H-2.sup.s) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. 14 days postinfection the animals were sacrificed and spleen cells were.

DETD . . . female C57BL/6j(H-2.sup.b) mice (Bomholtegaard, Ry) were given intravenous infections via the lateral tail vein with an inoculum of 5+10.sup.4 M. **tuberculosis** suspended in PBS in a vol. of 0.1 ml. After 1 month of infection the mice were treated with isoniazid.

.. . ++	+++	+	
rCFP29	+++	+++	++
rMPT51	+	-	-

Mouse IFN- $\gamma$  release during recall of memory immunity to M. **tuberculosis**.

-: no response;  
+: 1/3 of ST-CF;  
++: 2/3 of ST-CF;  
+++: level of ST-CF.

DETD . . . +++

rCFP21	+++
rCFP22	-
rCFP29	+
rCFP25	+++
rMPT51	+

Mouse IFN- $\gamma$  release 14 days after primary infection with M. **tuberculosis**.

-: no response;  
+: 1/3 of ST-CF;  
++: 2/3 of ST-CF;  
+++: level of ST-CF.

DETD . . . donors with no known exposure to patients with TB and from patients with culture or microscopy proven infection, with Mycobacterium **tuberculosis**. Blood samples were drawn from the TB patients 1-4 months after diagnosis.

DETD [0472] 6 weeks after the last immunization the mice were aerosol challenged with 5+10.sup.6 viable Mycobacterium **tuberculosis** /ml. After 6 weeks of infection the mice were killed and the number of viable bacteria in lung and spleen.

DETD [0476] Species distribution of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b as well as of cfp7a, cfp7b, cfp10a, cfp17, cfp21, cfp21, cfp22, cfp22a, cfp23, cfp25 and cfp25a.

DETD [0477] Presence of cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b in different mycobacterial species.

DETD [0478] In order to determine the distribution of the cfp7, cfp9, mpt51, rd1-orf2, rd1-orf3, rd1-orf4, **rd1-orf5**, rd1-orf8, rd1-orf9a and rd1-orf9b genes in species belonging to the M. **tuberculosis**-complex and in other mycobacteria PCR and/or



ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 2

Met Ser Gln Ile Met Tyr Asn Tyr Pro Ala Met Leu Gly His Ala Gly

1 5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 3

LENGTH: 467

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 3

gggtagccgg accacggctg ggcaaagatg tgcaggccgc catcaaggcg gtcaaggccg 60

gcgacggcgt cataaaccgc gacggcacct tggtggcggg ccccgcggtg ctgacgcccg 120

acgagtacaa ctcccggctg gtggccgccg acccgagatc caccgcggcg.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 4

LENGTH: 108

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 4

Met Ala Ala Asp Pro Glu Ser Thr Ala Ala Leu Pro Asp Gly Ala Gly

1 5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 5

LENGTH: 889

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 5

cgggtctgca cggatccggg ccgggcaggg caatcgagcc tgggatccgc tggggtgcgc 60

acatcgcgga cccgtgcgcg gtacggtcga gacagcggca cgagaaagta gtaagggcga 120

taataggcgg taaagagtag cgggaagccg gccgaacgac tcggtcagac.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 6

LENGTH: 162

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 6

Met Thr Asp Met Asn Pro Asp Ile Glu Lys Asp Gln Thr Ser Asp Glu

1 5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 7

LENGTH: 898

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 7

tcgactccgg cgccaccggg caggatcacg gtgtcgacgg ggtcgccggg gaatcccacg 60

ataaccactc ttcgcgccat gaatgccagt gttggccagg cgctggcctg gcgtccacgc 120

cacacaccgc acagattagg acacgccggc ggcgcagccc tgcccgaag.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 8

LENGTH: 165

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 8

Met Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu

1 5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 9

LENGTH: 1054

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 9

ataatcagct caccgttggg accgacctcg accaggggtc ctttgtgact gccgggcttg 60

acgcggacga ccacagagtc ggtcatcgcc taaggctacc gttctgacct ggggctgcgt 120

gggcgcggac gacgtgaggc acgtcatgtc tcagcggccc accgccacct.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 10

LENGTH: 217

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 10

Met Thr Pro Arg Ser Leu Val Arg Ile Val Gly Val Val Val Ala Thr

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 11

LENGTH: 949

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 11

agccgctcgc gtgggggtcaa ccgggtttcc acctgctcac tcattttgcc gcctttctgt 60

gtccggggccg aggcttgccg tcaataactc ggtcaagttc cttcacagac tgccatcact 120

ggcccgtcgg cgggctcgtt gcgggtgcgc cgcgtgcggg tttgtgttcc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 12

LENGTH: 182

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 12

Met Ala Asp Cys Asp Ser Val Thr Asn Ser Pro Leu Ala Thr Ala Thr

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 13

LENGTH: 1060

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 13

tggaccttca ccggcgttcc cttcgcttcg ggggcgacac ctaacatact ggtcgtcaac 60

ctaccgcgac accgctggga ctttgtgccca ttgccggcca ctccggggccg ctgcggcctg 120

gaaaaattgg tcgggcacgg gcggcccgcg gtcgctacca tccactgtg.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 14

LENGTH: 219

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 14

Met Gly Ala Ala Ala Met Leu Ala Ala Val Leu Leu Leu Thr Pro

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 15

LENGTH: 1198

TYPE: DNA

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 15

cagatgctgc gcaacatggt tctcggcgat ccggcaggca acaccgatcg agtgcttgac 60

ttttccaccg cggtgaccgg cggactgttc ttctcaccca ccatcgactt tctcgaccat 120

ccaccgcccc taccgcaggc ggcgacgcca actctggcag ccgggtcgt.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 16

LENGTH: 265

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

SEQUENCE: 16

Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 17

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium tuberculosis

FEATURE:

NAME/KEY: VARIANT

LOCATION: (1)

OTHER INFORMATION: Ala is Ala or Ser

SEQUENCE: 17

Ala Glu Leu Asp Ala Pro Ala Gln Ala Gly Thr.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 18

LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 18  
 Ala Gln Ile Thr Leu Arg Gly Asn Ala Ile Asn Thr Val Gly Glu  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 19  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (3)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 19  
 Asp Pro Xaa Ser Asp Ile Ala Val Val Phe Ala Arg Gly. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 20  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 20  
 Thr Asn Ser Pro Leu Ala Thr Ala Thr Ala Thr Leu His Thr Asn  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 21  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (2)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 21  
 Ala Xaa Pro Asp Ala Glu Val Val Phe Ala Arg Gly Arg. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 22  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (1)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 22  
 Xaa Ile Gln Lys Ser Leu Glu Leu Ile Val Val Thr Ala. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 23  
 LENGTH: 19  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 23  
 Met Asn Asn Leu Tyr Arg Asp Leu Ala Pro Val Thr Glu Ala Ala Trp  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 24  
 LENGTH: 34  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 24  
 cccggctcga gaacctstac cgcgacctsg csc  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 25  
 LENGTH: 37  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 25

gggccggatc cgasgcs gcg tccttsacs gytgcc	37
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 26	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 26	
ggaagcccca tatgaacaat ctctaccg	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 27	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 27	
cgcgctcagc ccttagtgac tgagcgcgac cg	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 28	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 28	
ctcgaattcg ccgggtgcac acag	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 29	
LENGTH: 25	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 29	
ctcgaattcg ccccatatcg agaac	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 30	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 30	
gtgtatctgc tggac	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 31	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 31	
ccgactggct ggccg	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 32	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 32	
gaggaattcg ctttagcgat cgca	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 33	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 33	
cccacattcc gttgg	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 34	
LENGTH: 15	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 34	
gtccagcaga tacac	15
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 35	
LENGTH: 27	
TYPE: DNA	

ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 35  
 gtacgagaat tcatgtcgca aatcatg 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 36  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 36  
 gtacgagaat tcgagcttgg ggtgccg 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 37  
 LENGTH: 28  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 37  
 cgattccaag cttgtggccg ccgacccg 28  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 38  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 38  
 cgttagggat cctcatcgcc atgggtgttg 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 39  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 39  
 cgttagggat ccggttccac tgtgcc 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 40  
 LENGTH: 28  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 40  
 cgttagggat cctcaggtct tttcgatg 28  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 41  
 LENGTH: 952  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 41  
 gaattcgccg ggtgcacaca gccttacacg acggaggtgg acacatgaag ggtcggtcgg 60  
 cgctgctgcg ggcgctctgg attgccgcac tgtcattcgg gttgggcggg gtcgcggtag 120  
 ccgcggaacc caccgccaag gccgccccat acgagaacct gatggtgccg.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 42  
 LENGTH: 299  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 42  
 Met Lys Gly Arg Ser Ala Leu Leu Arg Ala Leu Trp Ile Ala Ala Leu  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 43  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 43  
 gcaacacccg ggatgtcgca aatcatg 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 44  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 44

gtaacacccg gggtagccgc cgacccg 27  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 45  
LENGTH: 37  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 45  
ctactaagct tggatcccta gccgccccat ttggcg 37  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 46  
LENGTH: 38  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 46  
ctactaagct tccatgggtca ggtcttttcg atgcttac 38  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 47  
LENGTH: 450  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 47  
gtgccgcgct ccccaggggt cttatgggttc gatatacctg agtttgatgg aagtcgcatg 60  
accagcagtc agcatacggc atggccgaaa agagtggggg gatgatggcc gaggatgttc 120  
gcgccgagat cgtggccagc gttctcgaag tcgttgtaaa cgaaggcgat.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 48  
LENGTH: 71  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 48  
Met Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val  
1 5.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 49  
LENGTH: 750  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 49  
gggtacccat cgatggggtg cggttcggca ccgaggtgct aacgcacttg ctgacacact 60  
gctagtcgaa aacgaggcta gtcgcaacgt cgatcacacg agaggactga ccatgacaac 120  
ttacccegc cgtatgccg cgctgcccga gctgccgtcc ttcagcctga.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 50  
LENGTH: 176  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 50  
Met Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser  
1 5.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 51  
LENGTH: 800  
TYPE: DNA  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 51  
tcatgaggtt catcggggtg atcccacgcc cgcagccgca ttcggggccgc tggcgagccg 60  
gtgccgcacg ccgctcacc agcctgggtg ccgccgcctt tgcggcggcc acactgtgtg 120  
ttacccccgc gctggcacca ccggcatcgg cgggctgccc ggatgccgag.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 52  
LENGTH: 226  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 52  
Met Ile Pro Arg Pro Gln Pro His Ser Gly Arg Trp Arg Ala Gly Ala  
1 5.  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 53

LENGTH: 700  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 53  
 ctaggaaagc ctttcctgag taagtattgc cttcgttgca taccgccctt tacctgcgtt 60  
 aatctgcatt ttatgacaga atacgaaggg cctaagacaa aattccacgc gttaatgcag 120  
 gaacagattc ataacgaatt cacagcggca caacaatatg tcgcgatcgc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 54  
 LENGTH: 181  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 54  
 Met Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 55  
 LENGTH: 950  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 55  
 tgggctcggc actggctctc ccacgggtggc gcgctgattt ctccccacgg taggcgttgc 60  
 gacgcatggt cttcacgcgc tatccacagc taccgacatt tgctccggct ggatcgcggg 120  
 taaaattccg tcgtgaacaa tcgacccatc cgcttgctga catccggcag. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 56  
 LENGTH: 262  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 56  
 Met Asn Asn Arg Pro Ile Arg Leu Leu Thr Ser Gly Arg Ala Gly Leu  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 57  
 LENGTH: 1000  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 57  
 cgaggagacc gacgatctgc tcgacgaaat cgacgacgtc ctcgaggaga acgccgagga 60  
 cttcgctccgc gcatacgtcc aaaagggcgg acagtgacct ggccgttgcc cgatcgccctg 120  
 tccattaatt cactctctgg aacacccgct gtagacctat cttctttcac. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 58  
 LENGTH: 291  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 58  
 Met Thr Trp Pro Leu Pro Asp Arg Leu Ser Ile Asn Ser Leu Ser Gly  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 59  
 LENGTH: 900  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 59  
 ttggccccgc cgatcatcga aagccggttcg ggtgcggata ctttcggctc cgatggcggt 60  
 gagaagtgag ttttcggtat ttcattctgc ctgagcaggc gatgcgcgag cgcagcgagt 120  
 tggcgcgtaa gggcattgcg cgggccaaaa gcgtgggtggc gctggcctat. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 60  
 LENGTH: 248  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 60  
 Met Ser Phe Pro Tyr Phe Ile Ser Pro Glu Gln Ala Met Arg Glu Arg  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 61

LENGTH: 1560  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 61  
 gagtcattgc ctggtcggcg tcattccgta ctagtcgggt gtcggacttg acctactggg 60  
 tcaggccgac gagcactcga ccattagggt aggggccgtg acccactatg acgtcgtcgt 120  
 tctcggagcc ggtcccggcg ggtatgtcgc ggcgattcgc gccgcacagc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 62  
 LENGTH: 464  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 62  
 Met Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 63  
 LENGTH: 550  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 63  
 ggcccggctc gcggccgccc tgcaggaaaa gaaggcctgc ccaggcccag actcagccga 60  
 gtagtcaccc agtaccacac accaggaagg accgcccac atggcaaagc tctccaccga 120  
 cgaactgctg gacgcgttca aggaaatgac cctgttggag ctctccgact.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 64  
 LENGTH: 130  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 64  
 Met Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 65  
 LENGTH: 900  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 65  
 tgaacgcat cgggtccaac gaacgcagcg ctacctgatc accaccgggt ctgttagggc 60  
 tcttccccag gtctacagt cgggcatagg ccattgaggt ttcggtgttg cgggttttca 120  
 ccgattcaga cgggaatttc ggtaatccgc tgggggtgat caacgccagc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 66  
 LENGTH: 228  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 66  
 Met Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 67  
 LENGTH: 500  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 67  
 gtttggtgtg tcggtggtct ggggggcgcc aactgggatt cggttggggg ggggtgcaggt 60  
 ccggcgatgg gcatcgagg tgtgggtggg ttgggtgggg ccggttcggg tccggcgatg 120  
 ggcatggggg gtgtgggtgg tttgggtggg gccggttcgg gtccggcgat.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 68  
 LENGTH: 139  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 68  
 Met Gly Ala Gly Pro Ala Met Gly Ile Gly Gly Val Gly Gly Leu Gly  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 69

LENGTH: 2050  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 69  
 agcgactct gagaggtgt catggcggcc gactacgaca agctcttccg gccgcacgaa 60  
 ggatggaag ctccggacga tatggcagcg cagccgttct tcgaccccag tgcttcgttt 120  
 ccgccggcgc ccgcacgcgc aaacctaccg aagcccaacg gccagactcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 70  
 LENGTH: 666  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 70  
 Met Ala Ala Asp Tyr Asp Lys Leu Phe Arg Pro His Glu Gly Met Glu  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 71  
 LENGTH: 1890  
 TYPE: DNA  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 71  
 gcagcgatga ggaggagcgg cgccaacggc ccgcgccggc gacgatgcaa agcgacgcga 60  
 tgaggaggag cggcgcgcgc gactgctgaa ccggaagtac ggacgctgcg cgaggttgtg 120  
 ctggaccagc tcggcactgc tgaatcgcg. gctacaaga tgtggctgcc. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 72  
 LENGTH: 591  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 72  
 Met Thr Ala Glu Pro Glu Val Arg Thr Leu Arg Glu Val Val Leu Asp  
 1 5. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 73  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 SEQUENCE: 73  
 Asp Pro Val Asp Asp Ala Phe Ile Ala Lys Leu Asn Thr Ala Gly  
 1 5 10. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 74  
 LENGTH: 14  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (14)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 74  
 Asp Pro Val Asp Ala Ile Ile Asn Leu Asp Asn Tyr Gly. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 75  
 LENGTH: 15  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 FEATURE:  
 NAME/KEY: UNSURE  
 LOCATION: (5)  
 OTHER INFORMATION: Xaa is unknown  
 SEQUENCE: 75  
 Ala Glu Met Lys Xaa Phe Lys Asn Ala Ile Val Gln Glu. . .  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 76  
 LENGTH: 14  
 TYPE: PRT  
 ORGANISM: *Mycobacterium tuberculosis*  
 FEATURE:

NAME/KEY: VARIANT  
LOCATION: (3)  
OTHER INFORMATION: Ala is Ala or Gln  
SEQUENCE: 76  
Val Ile Ala Gly Met Val Thr His Ile His Xaa. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 77  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 77  
Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 78  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 78  
Ala Ile Glu Val Ser Val Leu Arg Val Phe Thr Asp Ser Asp Gly  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 79  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 79  
Ala Lys Leu Ser Thr Asp Glu Leu Leu Asp Ala Phe Lys Glu Met  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 80  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
FEATURE:  
NAME/KEY: VARIANT  
LOCATION: (4)  
OTHER INFORMATION: Asp is Asp or Glu  
SEQUENCE: 80  
Asp Pro Ala Asp Ala Pro Asp Val Pro Thr Ala. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 81  
LENGTH: 50  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 81  
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val  
1 5. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 82  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 82  
Thr Thr Ser Pro Asp Pro Tyr Ala Ala Leu Pro Lys Leu Pro Ser  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 83  
LENGTH: 15  
TYPE: PRT  
ORGANISM: Mycobacterium **tuberculosis**  
SEQUENCE: 83  
Thr Glu Tyr Glu Gly Pro Lys Thr Lys Phe His Ala Leu Met Gln  
1 5 10. . .  
DETD SEQUENCE CHARACTERISTICS:  
SEQ ID NO: 84  
LENGTH: 15  
TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 84

Thr Thr Ile Val Ala Leu Lys Tyr Pro Gly Gly Val Val Met Ala

1 5 10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 85

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (10)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 85

Ser Phe Pro Tyr Phe Ile Ser Pro Glu Xaa Ala Met Arg.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 86

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 86

Thr His Tyr Asp Val Val Val Leu Gly Ala Gly Pro Gly Gly Tyr

1 5 10

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 87

LENGTH: 450

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 87

agccccggtaa tcgagttcgg gcaatgctga ccatcggtt tgtttccggc tataaccgaa 60

cggtttgtgt acgggataca aatacagggg ggggaagaagt aggcaaattg aaaaaatgtc 120

acatgatccg atcgctgccg acattggcac gcaagtgagc gacaacgctc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 88

LENGTH: 98

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 88

Met Glu Lys Met Ser His Asp Pro Ile Ala Ala Asp Ile Gly Thr Gln

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 89

LENGTH: 460

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 89

gcaaccggct tttcgatcag ctgagacatc agcggcgtgc gggtaacga cccacctgcg 60

ccaggtagcg actccgcgcg cagcaggccc gcgccgcgc tggggcctga tccaccagcc 120

agcggatggt tcgacagcgg actgggtgcc agcaggccca tctgcgcggc.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 90

LENGTH: 139

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 90

Met Arg Val Asn Asp Pro Pro Ala Pro Gly Ser Asp Ser Ala Arg Ser

1 5

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 91

LENGTH: 1200

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 91

taataggccc ccaacacatc ggagggagtg atcaccatgc tgtggcacgc aatgccaccg 60

gagctaaata ccgcacggct gatggccggc gcgggtccgg ctccaatgct tgcggcggcc 120

gcgggatggc agacgctttc ggcggtcttg gacgctcagg ccgtcgagtt.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 92

LENGTH: 371  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 92  
 Met Ile Thr Met Leu Trp His Ala Met Pro Pro Glu Leu Asn Thr Ala  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 93  
 LENGTH: 1000  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 93  
 gacgcgacac agaaatcctt aaggccggcg gccaaaggggc cgaagggtgaa gaagggtgaag 60  
 ccccagaaac cgaaggccac gaagccgccc aaagtgggtgt cgcagcgcgg ctggcgacat 120  
 tgggtgcatg cgttgacgcg aatcaacctg ggctgtcac ccgacgagaa.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 94  
 LENGTH: 308  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 94  
 Met Lys Lys Val Lys Pro Gln Lys Pro Lys Ala Thr Lys Pro Pro Lys  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 95  
 LENGTH: 34  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 95  
 aagagtagat ctatgatggc cgaggatggt cgcg 34  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 96  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 96  
 cggcgacgac ggatcctacc gcgtcgg 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 97  
 LENGTH: 28  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 97  
 ccttgggaga tctttggacc ccggttgc 28  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 98  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 98  
 gacgagatct tatgggctta ctgac 25  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 99  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 99  
 cccccagat ctgcaccacc ggcacgcggcg ggc 33  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 100  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 100  
 gcggcggatc cgttgcttag ccgg 24  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 101  
 LENGTH: 32

TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 101	
ccggctgaga tctatgacag aatacgaagg gc	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 102	
LENGTH: 24	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 102	
ccccgccagg gaactagagg cggc	24
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 103	
LENGTH: 38	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 103	
ctgccgagat ctaccacat tgtcgcgctg aaataccc	38
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 104	
LENGTH: 25	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 104	
cgccatggcc ttacgcgcca actcg	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 105	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 105	
ggcggagatc tgtgagtttt ccgtatttca tc	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 106	
LENGTH: 25	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 106	
cgcgtcgagc catggtagg cgcag	25
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 107	
LENGTH: 32	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 107	
gaggaagatc tatgacaact tcacccgacc cg	32
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 108	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 108	
catgaagcca tggcccgcag gctgcatg	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 109	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 109	
ggccgagatc tgtgaccac tatgacgtcg tcg	33
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 110	
LENGTH: 36	
TYPE: DNA	
ORGANISM: Mycobacterium <b>tuberculosis</b>	
SEQUENCE: 110	
ggcgcccatg gtcagaaatt gatcatgtgg ccaacc	36
DETD SEQUENCE CHARACTERISTICS:	

SEQ ID NO: 111  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 111  
 ccgggagatc tatggcaaag ctctccaccg acg 33  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 112  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 112  
 cgctgggcag agctacttga cggtgacggt gg 32  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 113  
 LENGTH: 36  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 113  
 ggcccagatc tatggccatt gaggtttcgg tgttgc 36  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 114  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 114  
 cgccgtgttg catggcagcg ctgagc 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 115  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 115  
 ggacgttcaa gcgacacatc gccg 24  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 116  
 LENGTH: 24  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 116  
 cagcacgaac gcgccgtcga tggc 24  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 117  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 117  
 acagatctgt gacggacatg aacccg 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 118  
 LENGTH: 28  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 118  
 ttttccatgg tcacgggccc ccggtact 28  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 119  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 119  
 acagatctgt gcccatggca cagata 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 120  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 120

tttaagcttc taggcgcca gcgcggc	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 121	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 121	
acagatctgc gcatcgcat ccgtgt	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 122	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 122	
ttttccatgg tcatccggcg tgatcgag	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 123	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 123	
acagatctgt aatggcagac tgtgat	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 124	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 124	
ttttccatgg tcaggagatg gtgatcga	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 125	
LENGTH: 26	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 125	
acagatctgc cggctacccc ggtgcc	26
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 126	
LENGTH: 28	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 126	
ttttccatgg ctattgcagc tttccggc	28
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 127	
LENGTH: 50	
TYPE: PRT	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 127	
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val	
1 5 . . .	
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 128	
LENGTH: 49	
TYPE: PRT	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 128	
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val	
1 5 . . .	
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 129	
LENGTH: 50	
TYPE: PRT	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 129	
Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val	
1 5 . . .	
DETD SEQUENCE CHARACTERISTICS:	

SEQ ID NO: 130  
 LENGTH: 33  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 130  
 ccgggagatc tatggcaaag ctctccaccg acg 33  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 131  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 131  
 cgctgggcag agctacttga cggtgacggg gg 32  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 132  
 LENGTH: 36  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 132  
 ggcgccggca agcttgccat gacagagcag cagtgg 36  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 133  
 LENGTH: 26  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 133  
 cgaactcgcc ggatcccgtg tttcgc 26  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 134  
 LENGTH: 32  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 134  
 ggcaaccgcg agatctttct cccggccggg gc 32  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 135  
 LENGTH: 27  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 135  
 ggcaagcttg ccggcgccta acgaact 27  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 136  
 LENGTH: 30  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 136  
 ggaccagat ctatgacaga gcagcagtgg 30  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 137  
 LENGTH: 47  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 137  
 ccggcagccc cggccgggag aaaagctttg cgaacatccc agtgacg 47  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 138  
 LENGTH: 44  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 138  
 gttcgcaaag cttttctccc ggccgggggct gccggtcgag tacc 44  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 139  
 LENGTH: 20  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 139

ccttcggtgg atccccgtcag 20  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 140  
 LENGTH: 450  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 140  
 tggcgctgtc accgaggaac ctgtcaatgt cgtcgagcag tactgaaccg ttccgagaaa 60  
 ggccagcatg aacgtcaccg tatccattcc gaccatcctg cggccccaca ccggcggcca 120  
 gaagagtgtc tcggccagcg gcgatacctt gggtgccgtc atcagcgacc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 141  
 LENGTH: 93  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 141  
 Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 142  
 LENGTH: 480  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 142  
 ggtgttcccc cggccggcta tgacaacagt caatgtgcat gacaagttac aggtattagg 60  
 tccaggttca acaaggagac aggcaacatg gcaacacgtt ttatgacgga tccgcacgcg 120  
 atgcgggaca tggcgggccc ttttgaggtg cacgcccaga cggtgaggaga.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 143  
 LENGTH: 98  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 143  
 Met Ala Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 144  
 LENGTH: 940  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 144  
 gccccagtc tcatcgccct catcgccctc accggccgcc agccgaccgc aggccacgtg 60  
 tccgccacct aacgaaagga tgatcatgcc caagagaagc gaatacaggc aaggcacgcc 120  
 gaactgggtc gaccttcaga ccaccgatca gtccgccgcc aaaaagttct.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 145  
 LENGTH: 261  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 145  
 Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp  
 1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 146  
 LENGTH: 280  
 TYPE: DNA  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 146  
 ccgaaaggcg gtgcaccgca cccagaagaa aaggaaagat cgagaaatgc cacagggaac 60  
 tgtgaagtgg ttcaacgcgg agaaggggtt cggctttatc gccccgaag acggttccgc 120  
 ggatgtattt gtccactaca cggagatcca gggaaacgggc ttccgcaccc.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 147  
 LENGTH: 67  
 TYPE: PRT  
 ORGANISM: Mycobacterium tuberculosis  
 SEQUENCE: 147  
 Met Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly

1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 148  
 LENGTH: 540  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 148  
 atcgtgtcgt atcgagaacc ccggccggta tcagaacgcg ccagagcgca aacctttata 60  
 acttcgtgtc ccaaagtgtga cgaccatgga ccaaggttcc tgagatgaac ctacggcgcc 120  
 atcagaccct gacgctgcga ctgctggcgg catccgcggg cattctcagc.

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 149  
 LENGTH: 129  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 149  
 Met Asn Leu Arg Arg His Gln Thr Leu Thr Leu Arg Leu Leu Ala Ala

1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 150  
 LENGTH: 400  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 150  
 atagtttggg gaagggtgcc ataaatgagg ctgtcgttga ccgcattgag cgccgggtgta 60  
 ggcgccgtgg caatgtcgtt gaccgtcggg gccggggtcg cctccgcaga tcccgtggac 120  
 gcggtcatta acaccacctg caattacggg caggtagtag ctgcgctcaa.

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 151  
 LENGTH: 110  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 151  
 Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala Val Ala

1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 152  
 LENGTH: 990  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 152  
 aatagtaata tcgctgtgcg gttgcaaaac gtgtgaccga gggtccgcag tcgagcgctg 60  
 cgggccgcct tcgaggagga cgaaccacag tcatgacgaa catcgtggtc ctgatcaagc 120  
 aggtcccaga tacctggtcg gagcgcaagc tgaccgacgg cgatttcacg.

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 153  
 LENGTH: 266  
 TYPE: PRT  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 153  
 Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser

1 5.  
 DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 154  
 LENGTH: 25  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 154  
 ctgagatcta tgaacctacg gcgcc 25

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 155  
 LENGTH: 35  
 TYPE: DNA  
 ORGANISM: Mycobacterium **tuberculosis**  
 SEQUENCE: 155  
 ctcccatggg accctaggac ccgggcagcc ccggc 35

DETD SEQUENCE CHARACTERISTICS:  
 SEQ ID NO: 156

LENGTH: 29	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 156	
ctgagatcta tgaggctgtc gttgaccgc	29
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 157	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 157	
ctccccgggc ttaatagttg ttgcaggagc	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 158	
LENGTH: 33	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 158	
gcttagatct atgattttct gggcaaccag gta	33
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 159	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 159	
gcttccatgg gcgaggcaca ggcgtgggaa	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 160	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 160	
ctgagatcta gaatgccaca gggaaactgtg	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 161	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 161	
tctccccgggg gtaactcaga gcgagcggac	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 162	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 162	
ctgagatcta tgaacgtcac cgtatcc	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 163	
LENGTH: 27	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 163	
tctccccgggg ctcacccacc ggccacg	27
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 164	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 164	
ctgagatcta tggcaacacg ttttatgacg	30
DETD SEQUENCE CHARACTERISTICS:	
SEQ ID NO: 165	
LENGTH: 30	
TYPE: DNA	
ORGANISM: Mycobacterium tuberculosis	
SEQUENCE: 165	
ctccccgggt tagctgctga ggatctgcth	30

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 166

LENGTH: 31

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 166

ctgaagatct atgcccaaga gaagcgaata c

31

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 167

LENGTH: 31

TYPE: DNA

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 167

cggcagctgc tagcattctc cgaatctgcc g

31

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 168

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 168

Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly

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10.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 169

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: UNSURE

LOCATION: (15)

OTHER INFORMATION: Xaa is unknown

SEQUENCE: 169

Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 170

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

FEATURE:

NAME/KEY: VARIANT

LOCATION: (1)

OTHER INFORMATION: Thr could also be Ala

SEQUENCE: 170

Thr Arg Phe Met Thr Asp Pro His Ala Met Arg.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 171

LENGTH: 15

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 171

Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp

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10.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 172

LENGTH: 404

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 172

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His

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5.

DETD SEQUENCE CHARACTERISTICS:

SEQ ID NO: 173

LENGTH: 403

TYPE: PRT

ORGANISM: Mycobacterium **tuberculosis**

SEQUENCE: 173

Met Ala Thr Val Asn Arg Ser Arg His His His His His His His

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CLM

What is claimed is:

in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, or c) comprises an amino acid sequence having a sequence identity with the polypeptide defined in a) or the . . . in a) with respect to the ability of evoking a protective immune response against infections with mycobacteria belonging to the **tuberculosis** complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the **tuberculosis** complex, with the proviso that i) the polypeptide fragment is in essentially pure form when consisting of the amino acid.

weeks of primary infection or within 4 days after the mouse has been rechallenged infected with mycobacteria belonging to the **tuberculosis** complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200.000 spleen cells per ml, . . . suspension; and/or 3) induces an IFN- $\gamma$  release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the **tuberculosis** complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the **tuberculosis** complex.

fragment as defined in any of claims 1-8, and an other polypeptide fragment derived from a bacterium belonging to the **tuberculosis** complex, such as ESAT-6 or at least one T-cell epitope thereof, MPB64 or at least one T-cell epitope thereof, MPT64.

first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein ESAT-6, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from ESAT-6 and/or including a stretch of amino acids which protects the first amino acid sequence from in. . . first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. **tuberculosis** protein MPT59, and a second amino acid sequence including at least one T-cell epitope derived from a M. **tuberculosis** protein different from MPT59 and/or including a stretch of amino acids which protects the first amino acid sequence from in.

11-13, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-55, DnaK, GroEL, urease, glutamine.

sequence of ESAT-6 or of MPT59 and/or the second amino acid sequence is the amino acid sequence of a M. **tuberculosis** polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-8, DnaK, GroEL, urease, glutamine.

according to any of claims 1-20 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the **tuberculosis** complex in an animal, including a human being.

according to claim 23 or 24 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against **tuberculosis** caused by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*.

35. A vaccine for immunizing an animal, including a human being, against

**tuberculosis** caused by mycobacteria belonging to the **tuberculosis** complex, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a DNA fragment comprising a . . .

44. A transformed cell according to claim 43, which is a bacterium belonging to the **tuberculosis** complex, such as a M. **tuberculosis** bovis BCG cell.

. . . polypeptide from a short-term culture filtrate as defined in claim 1; or isolating the polypeptide from whole mycobacteria of the **tuberculosis** complex or from lysates or fractions thereof, e.g. cell wall containing fractions; or synthesizing the polypeptide by solid or liquid.

. . . of claims 1-20, and solubilizing or dispersing the polypeptide in a medium for a vaccine, and optionally adding other M. **tuberculosis** antigens and/or a carrier, vehicle and/or adjuvant substance, or cultivating a cell according to any of claims 37-45, and transferring.

48. A method of diagnosing **tuberculosis** caused by Mycobacterium **tuberculosis**, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide. . . composition according to claim 34, a positive skin response at the location of injection being indicative of the animal having **tuberculosis**, and a negative skin response at the location of injection being indicative of the animal not having **tuberculosis**

49. A method for immunising an animal, including a human being, against **tuberculosis** caused by mycobacteria belonging to the **tuberculosis** complex, comprising administering to the animal the polypeptide according to any of claims 1-20, the immunologic composition according to claim. . .

. . . A method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the **tuberculosis** complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the. . .

52. A composition for diagnosing **tuberculosis** in an animal, including a human being, comprising a polypeptide according to any of claims 1-20, or a nucleic acid. . .

L13 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of Mycobacterium **tuberculosis** culture filtrates

and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin;

Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	CA 2285625	AA	19981008	CA 1998-2285625	19980401

AU 9868204	A1	19981022	AU 1998-68204	19980401
AU 740545	B2	20011108		
EP 972045	A1	20000119	EP 1998-913536	19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515359	T2	20010918	JP 1998-541074	19980401
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CA 2319380	AA	19990520	CA 1998-2319380	19981008
WO 9924577	A1	19990520	WO 1998-DK438	19981008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1029053	A1	20000823	EP 1998-947412	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 504951	A	20010629	NZ 1998-504951	19981008
AU 750173	B2	20020711	AU 1998-94338	19981008
EP 1484405	A1	20041208	EP 2004-77071	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
EP 1998-913536	A3	19980401		
WO 1998-DK132	W	19980401		
EP 1998-947412	A3	19981008		
WO 1998-DK438	W	19981008		

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a  $\lambda$ gt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel antigens of *Mycobacterium tuberculosis* culture filtrates and the genes encoding and their diagnostic and prophylactic use

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a  $\lambda$ gt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

ST *Mycobacterium* culture filtrate antigen gene; vaccine *tuberculosis*  
*Mycobacterium* antigen gene

IT Lipoproteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(19 kDa, as antigen of *Mycobacterium tuberculosis*, fusion proteins containing; novel antigens of *Mycobacterium tuberculosis* culture filtrates and genes encoding and their diagnostic and

prophylactic use)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (85 complex, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (DnaK, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ESAT6, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (GroEL, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Chaperonins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (GroES, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT51, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT59, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (MPT64, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antigens  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
 (culture filtrate antigens of Mycobacterium; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**  
 (diagnosis, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Escherichia  
Mycobacterium  
Mycobacterium BCG  
Pseudomonas  
Salmonella  
(expression host for Mycobacterium **tuberculosis** antigen genes; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Hemagglutinins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(heparin-binding, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium **tuberculosis**  
(novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Molecular cloning  
(of antigen genes of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Fusion proteins (chimeric proteins)  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(of antigens of Mycobacterium **tuberculosis**, for vaccines; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Protein sequences  
(of antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT DNA sequences  
(of genes for antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pRVN01, expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pRVN02, expression vector for antigen genes of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pT087, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pT088, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pT089, gene for antigen of Mycobacterium **tuberculosis** on; novel antigens of Mycobacterium **tuberculosis** culture

filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pTO90, gene for antigen of Mycobacterium **tuberculosis** on;  
novel antigens of Mycobacterium **tuberculosis** culture  
filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pTO91, gene for antigen of Mycobacterium **tuberculosis** on;  
novel antigens of Mycobacterium **tuberculosis** culture  
filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pTO96, gene for antigen of Mycobacterium **tuberculosis** on;  
novel antigens of Mycobacterium **tuberculosis** culture  
filtrates and genes encoding and their diagnostic and prophylactic use)

IT Plasmid vectors  
(pTO98, gene for antigen of Mycobacterium **tuberculosis** on;  
novel antigens of Mycobacterium **tuberculosis** culture  
filtrates and genes encoding and their diagnostic and prophylactic use)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(phosphate-binding, as antigen of Mycobacterium **tuberculosis**,  
fusion proteins containing; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(proline-rich, as antigen of Mycobacterium **tuberculosis**,  
fusion proteins containing; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf2, for antigen of Mycobacterium **tuberculosis**; novel  
antigens of Mycobacterium **tuberculosis** culture filtrates and  
genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf3, for antigen of Mycobacterium **tuberculosis**; novel  
antigens of Mycobacterium **tuberculosis** culture filtrates and  
genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf4, for antigen of Mycobacterium **tuberculosis**; novel  
antigens of Mycobacterium **tuberculosis** culture filtrates and  
genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf5, for antigen of Mycobacterium  
**tuberculosis**; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf8, for antigen of Mycobacterium **tuberculosis**; novel  
antigens of Mycobacterium **tuberculosis** culture filtrates and  
genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(rd1-orf9a, for antigen of Mycobacterium **tuberculosis**; novel  
antigens of Mycobacterium **tuberculosis** culture filtrates and  
genes encoding and their diagnostic and prophylactic use)

IT Gene, microbial  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rdl-orf9b, for antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Antibodies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (to antigens of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Mycobacterium africanum  
 Mycobacterium bovis  
 (**tuberculosis** caused by; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Diagnosis  
 (**tuberculosis**, vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Vaccines  
 (**tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT **Tuberculosis**  
 (vaccines against and diagnosis of; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT Crystallins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( $\alpha$ -, as antigen of Mycobacterium **tuberculosis**, fusion proteins containing; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 213992-07-5 213992-08-6 213992-09-7D, amino acid-substituted analogs  
 213992-10-0 213992-11-1 213992-12-2 213992-13-3 213992-14-4  
 213992-15-5 213992-16-6 213992-17-7 213992-18-8 213992-19-9  
 213992-20-2 213992-21-3 213992-22-4 213992-23-5 213992-24-6  
 214072-43-2 214072-44-3 214072-45-4 214072-46-5 214072-47-6  
 214142-58-2  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (N-terminal peptide of Mycobacterium **tuberculosis** antigen; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 151185-45-4, Protein (Mycobacterium BCG strain Tokyo ribosome)  
 208778-78-3 208782-67-6 208783-23-7 208783-90-8 208786-90-7  
 208788-06-1 208788-47-0 208790-41-4 208790-42-5 208853-48-9  
 208856-86-4 208857-49-2 208859-77-2 208863-45-0 208864-30-6  
 208865-40-1 208868-63-7 208871-19-6 208872-79-1 208874-21-9  
 208875-49-4 209053-74-7 210170-05-1 214348-60-4 214348-78-4  
 214348-84-2 214348-92-2 214349-12-9 214349-22-1 214349-24-3  
 214349-26-5 214349-38-9  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT 9002-13-5D, Urease, fusion products 9023-70-5D, Glutamine synthetase, fusion products 9029-06-5D, Alanine dehydrogenase, fusion products 9054-89-1D, Superoxide dismutase, fusion products  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (as antigen of Mycobacterium **tuberculosis**; novel antigens of Mycobacterium **tuberculosis** culture filtrates and genes encoding and their diagnostic and prophylactic use)

IT	214348-46-6	214348-59-1	214348-61-5	214348-62-6	214348-68-2
	214348-69-3	214348-70-6	214348-76-2	214348-77-3	214348-79-5
	214348-80-8	214348-81-9	214348-82-0	214348-83-1	214348-85-3
	214348-86-4	214348-88-6	214348-89-7	214348-90-0	214348-91-1
	214348-93-3	214349-11-8	214349-21-0	214349-23-2	214349-25-4
	214349-28-7	214349-47-0	214349-53-8	214349-54-9	214349-57-2
	214349-60-7	214349-62-9	214349-63-0		

RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; novel antigens of Mycobacterium  
**tuberculosis** culture filtrates and genes encoding and their  
diagnostic and prophylactic use)